Review Paper:

Risk factors and preventive measures for basal cells carcinoma in India

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Abstract

In a developing country like India, Basal cell carcinoma (BCC) is very common. Invasive and pre-invasive lesions are generally formed during BCC. In this study comprehend the pertaining epidemiology, pathogenesis and the risk factors associated to the BCC and related prevention methods to be acquired. The "morphological and molecular pathways" in understanding the occurrence of low-grade breast cancers were studied by the association and immune-profile of commonly acquire lesions including ADH "(atypical ductal hyperplasia), DCIS (ductal in situ carcinoma), LN Columnar CCL lesions and Ul Epithelial Hyperplasia (UEH) lesions.

By applying FNAC, microscopically, immunochemistry and histopathologic techniques, it is found that more than 80% of patients have low-grade IDC, TC, TLC and cribriform associated CCLs. In 90% patients of ILCs performed and immunohistochemistry, LN occurred only in few cases (15%) of ILCs. For CK19/18/8, ER-like, Bcl-2, and D-1 cycline were involved in columnar cell hyperplasia (CCH) with cells expressing ER-relevant increasing with atypia. CCLs, particularly FEA, are found very frequently in the low grade of breast carcinoma. For low-grade breast neoplasia, CK19/18/8 +, ER-and Bcl-2 + are the major progenitor cells.

Keywords: BCC, DCIS, IDC, TC, TLC.

Introduction

"Rodent ulcer" word was coined by Jacob Arthurin in 1827 to describe what we now know as BCC[1]. It is the most common skin malignancy worldwide, comprising 65–75% of all skin cancers. Significant disparities are reported in the percentage of skin cancer in Asians (2–4%) and Blacks (1-2%) relative to Caucasians (35–40%)[2]. Although the incidence of skin cancers in India is lower than in the Western world, due to large population, absolute numbers of cases may be significant. Current BCC literature in India is scarce with lack of systematic review clinical studies[3]. This research was undertaken to fill this gap in BCC literature based on risk factors and disease prevention measures. BCC is a nonmelanocytic skin malignancy resulting from epidermis or follicular basal cells and is seen mainly on sun-exposed areas, particularly the head and neck, sometimes over the trunk and limbs, and rarely on hands, soles, mucous membranes and genitals[4,5]. BCC's anatomic distribution coincides with fusion planes. Recently, BCC incidence was documented to be higher along embryonic fusion planes compared to other midface areas.[6] Basal cell carcinoma (BCC) forms to be extremely common and its incidences are ever rising. There are two broad categories asseverating carcinoma in the breast and carcinoma of anal region. Ninety-five percent of these neoplasms occur in patients over 40 years of age, while infant and congenital basal cell epitheliomas were reported[7–9].

In infants, genetic defects such as basal cell nevus syndrome, xeroderma pigmentosum, nevus sebaceous, epidermodysplasia verruciformis, Rombo syndrome, or Bazex syndrome are typically involved. Sunlight is the most common association with BCC development; risk correlates with cumulative exposure, particularly during childhood. A 20–50-year latency duration is common between ultraviolet (UV) damage and clinical onset of BCC. Both UVB and UVA radiation contribute to BCC formation. UVB plays a greater role in BCC production than UVA[10]. In 2012, systematic review and meta-analysis of 12 studies involving 9328 cases of nonmelanoma skin cancer, Wehner et al[30] found that indoor tanning was associated with substantially higher risk of both basal and squamous skin cancer and the highest risk among indoor tanning users before age twenty five[11].

In addition to UVR, ray exposure is also associated with BCC growth. Arsenic has been used as a therapeutic agent, specifically the Fowler potassium arsenite solution and has been used to treat many conditions including asthma and psoriasis and is related to the possibility of multiple malignancies after long years of delay. The risk of developing new nonmelanoma skin cancer is estimated to be 35% at 3 years and 5% after an initial skin cancer diagnosis[12].

A research among U.S. adults reported a clear correlation between excessive alcohol drinking and higher incidence of sunburn indicating a connection between alcohol consumption and skin cancer[13]. This study aims to comprehend the pertaining epidemiology, pathogenesis and the risk factors associated to the BCC and related prevention methods to be acquired for the same. The study takes into

consideration the "morphological and molecular pathways" in understanding the occurrence of low-grade breast cancers by studying the association and immune-profile of commonly acquire lesions including ADH "(atypical ductal hyperplasia), DCIS (ductal *in situ* carcinoma), LN Columnar CCL lesions and Ul Epithelial Hyperplasia (UEH) lesions.

Major risk factors of BCC: Major risk factors pertaining to occurrence of BCC can be classified into four categories: first, the physical characters, secondly exposure to external sources, thirdly genetics and fourthly immunosuppression. The acquired physical characters like blond or red hair, blue or green eyes, light skin color are vulnerable traits risking BCC. Exposure to certain external elements like Arsenic, Coal tar, Ionizing radiation, Smoking, Tanning-bed and Ultraviolet light can also induce risk of BCC to major extent. Some heavy metals, metalloids and pesticides can act as carcinogenic agents for human beings.[14-16] Some of the genetic deficiencies like Albinism, Xeroderma pigmentosum (XP), Gorlin syndrome (nevoid BCC) may also stimulate the risk of BCC to a certain degree. Risk to the occurrence of BCC can also be associated with counteractive response of organ transplantation recipients.

Prevention measures: There are no definitive ways to avoid BCC, but only certain measures can be taken to reduce possible risks such as increasing shade and other incentives for sun safety in outdoor recreational settings, encouraging safe UV exposure choices, supporting policies that advance the national goal of skin cancer prevention, minimizing indoor tanning harms, strengthening research, surveillance, monitoring, and evaluation related to skin cancer prevention[17].

Design: Many studies have reported that both invasive and pre-invasive lesions have been subjected to microscopic analysis in "100 low-grade breast tumors forming low-grade IDC[18], cribriform[19], pure and tubular (TC)[20], tubulolobular (TLC)[21] and classic ILC[22]. Immunohistochemically tissue microarrays containing 1100 lessons for tumor suppression have also been performed[23,24].

In this study, all the available hematoxylin and eosin-stained histologic sections of invasive low and high nuclear grade carcinoma were removed by simple mastectomy. The first line screening method- Fine needle aspiration cytology (FNAC) is used which is normally recommended in suspected malignancy[25,26] and presence of granulomata in an aspirate may indicate the presence of a neoplastic process, then smear was examined microscopically.

The presence of invasive and preinvasive lesions including CCLs, IDC, TC, TLC, DCIS, and LN was determined. For the purpose of this study, atypical lobular hyperplasia and lobular carcinoma *in situ* were grouped together under LN. A comprehensive morphologic review of CCLs was performed based on the classification system outlined by Schnitt and Vincent-Salmon[27,28]. At the end results of FNAC, molecular techniques are reviewed and analysed along with the final histological diagnosis and medical history of patient.

Morphology: It has been found that more than 80% of low-grade IDC, TC, TLC and cribriform associated CCLs with high-grade flat epithelial atypia (FEA),CCL, DCIS and invasive lessons were responsible for more patients; in 90% of ILCs, immunohistochemistry, LN occurred only in a few cases (15%) capsized with ILCs; for CK19/18/8, ER-like, Bcl-2, and D-1 cycline were involved in columnar cell hyperplasia (CCH) with cells expressing ER-relevant increasing with atypia. Observation of ER- range / ER- and Cycline D-1 was found on carcinogenesis of higher side duration. Further, Bcl-2 detected carcinoma-related CCLs, ADH, LN and low-grade DCIS in the epithelial lining cells.

From the study conducted, it is evident that CCLs, particularly FEA, are found very frequently in the low grade of breast Carcinoma and ILC, which represent community of precursors containing "invasive neoplastic and situ" lesions in the "A" luminal subclass. As shown by our laboratory findings, CK19/18/8 +, ER-and Bcl-2 + are the major progenitor cells for low-grade breast neoplasia. When driving cycline D-1, Bcl2, the distinction between ER-affected / ER-expression could be very useful.

On the other hand, the stem/ progenitor cells of breast cancer' irrespective of their original phenotype receive early stochastic genetic / epigenetic hits, resulting in the activation of the luminal. A pathway (ER / cycline D1 pathways) is considerate of pre invasive and invasive lesion phenotype. It has been observed that if cells respond with this molecular pathway, progression to a 'high grade' phenotype (basal-like or HER2) is unlikely.

Low-grade IDC, TC, ICC, classic ILC and TLC all have a relatively favorable prognosis possibly because of high levels of differentiation which may be the consequence of fewer genetic aberrations[29]. In a recent study, we reported a high frequency of coexistence of CCLs, ADH/low-grade DCIS and LN, with TC, TLC and ILC respectively suggesting that these lesions are members of a single family of low-grade precursor *in situ* and invasive neoplastic lesions of the breast[27]. In our study we found that LN occurred only in a few cases (15%) capsized with ILCs; For CK19/18/8, ER-like, Bcl-2 and D-1 cycline are involved in columnar cell hyperplasia (CCH) with cells expressing ER-relevant, increasing with atypia. Observation of ER- range / ER- and Cycline D-1 was found on carcinogenesis of higher side duration.

Further, Bcl-2 detected carcinoma-related CCLs, ADH, LN and low-grade DCIS in the epithelial lining cells. While Abdel-Fatah et al[1] suggested that in contrast, FEA, ADH/low-grade DCIS and LN were consistently negative for CK5/6, CK14 and vimentin and positive for ER-α, Bcl-2, cyclin D1, and CK19/18/8. Further in our result,

Bcl-2 detected carcinoma-related CCLs, ADH, LN and low-grade DCIS in the epithelial lining cells. CK19/18/8 +, ER- and Bcl-2 + are the major progenitor cells for low-grade breast neoplasia. A pathway (ER / cycline D1 pathways) is considerate of pre invasive and invasive lesion phenotype. It has been observed that if cells respond with this molecular pathway, progression to a 'high grade' phenotype (basal-like or HER2) is unlikely.

Scope for future intervention: Government agencies, NGOs and social media will play an important role in spreading useful knowledge with regards to spread of BCC. Awareness and campaigns in local language have to be in place in both urban and rural area to minimize the risk of breast cancer. Further, carcinoma syllabus, in an attempt to acquaint the medical professionals with regard to carcinoma must be in place concentrating on methods of breast detection and screening. Women in the late thirties must necessarily undergo general screening in India for breast carcinoma, as breast carcinoma is often seen in younger age groups.

Appropriate surgical management and referral CMEs can play a major role in acquainting the basic breast surgery skills for the general surgeons. Guidelines for procedures for breast carcinomas were created for the developing countries. India has, however a limited resource and economic, social and health gaps. Our own management guidelines must therefore be formulated which are feasible and practical. Regulation by regulatory authorities with regards to the cost of chemotherapy medications is of vital importance in providing patients with full care. Further genetic techniques are required for early detection of breast cancer in India. Mobile mammography units aimed at determining women's health are crucial to be set up in country's interior, towns, hilly areas etc.

Conclusion

From this study it can be concluded that more than 80% of patients have low-grade IDC, TC, TLC and cribriform associated CCLs. In 90% patients of ILCs performed and immune-histochemistry, LN occurred only in a few cases (15%) of ILCs. For CK19/18/8, ER-like, Bcl-2, and D-1 cycline were involved in columnar cell hyperplasia (CCH) with cells expressing ER-relevant, increasing with atypia. CCLs, particularly FEA, are found very frequently in the low grade of breast carcinoma.

For low-grade breast neoplasia, CK19/18/8 +, ER-and Bcl-2 + are the major progenitor cells. As stem cells receive early stochastic genetic / epigenetic hits resulting in the activation of the luminal. ER / cycline D1 pathways inhibit progression to a 'high grade' phenotype (basal-like or HER2).

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(Received 22nd September 2020, accepted 17th November 2020)

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