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Non-melanoma skin cancer: contributory factors, treatment, and prevention

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Abstract:*Non-melanoma skin cancers (NMSC), and melanoma skin cancer is prevalent worldwide. Melanoma has high mortality. Australia and New Zealand have the highest rates of melanoma in the world. Disease is more common in areas which are more Caucasian. Ultraviolet radiation from sun exposure is the primary contributory factor. Genetic syndrome, ionizing radiation, light skin, and tanning beds are also the cause basal-cell and squamous-cell skin cancer. Basal-cell carcinoma (BCC) appears as painless raised area, squamous-cell carcinoma(SCC) presents as a hard lump with scaly top but may also form an ulcer, and malignant melanoma appear as a mole that has changed size,shape,,color, has irregular edges, itchy or bleeds. Melanomaare most aggressive.Treatment of skin cancer dependent on type, location, age of the patient and whether cancer is primary or recurrence.Moh'smicrograph surgery is the surgery of choice. Plastic or reconstructive surgery may be indicated.BCC and SCC have better prognosis. Survival of people with melanoma depends upon when they start treatment. Better outcome when detected in the early stages. Sunscreen is effective and is recommended to prevent melanoma.*
Keywaords;*Skin cancer,Contributory factors,Treatment*

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I. Introduction

Non-melanoma skin cancers (NMSC) arise from the skin.They are due to the development of abnormal cells that have the ability to invade or spread to other parts of the body[1].There are three main types of skin cancers: basal-cell-skin cancer (BCC), squamous-cell skin cancer(SCC) and melanoma[2].Skin cancer is most common form of cancer, globally accounting for at least 40% of cases[3].NMSC is the most common type of cancer, which occurs in at least 2.3 million people per year[4].in 2015, 5.6 million people were affected[5],with 111,700 deaths[6].0f NMSCs,about 80% are basal-cell cancers and 20% squamous cell skin cancers. BCC and SCC rarely result in death[4].Globally in 2012 melanoma occurred in 232,000 people and resulted in 55,000 deaths[4].Australia and New Zealand have the highest rates of melanoma in the world[4].The three main types of skin cancer have become more common in the last 20 to 40 years, especially in those areas which are mostly Caucasian[4].Greater than 90% of cases are caused by exposure to ultraviolet radiation from the sun, and tanning beds are becoming another common source of ultraviolet radiation[7].People with light skin are at higher risk[2], as are those with poor immune function such as from medication or HIV/AIDS [3].Clinical manifestation in BCC :painless raised area of the skin that may be shiny with small blood vessel running over it or ulceration[2],in SCC a hard lump with scaly top[8], and in melanoma: mole that has changed in size, shape, color or has irregular edges[9].For melanoma and basal-cell cancers exposure during childhood is particularly harmful[4].Diagnosis by biopsy[7].Treatment by surgery, radiation therapy and topical medication such as fluorouracil[2].Prevention by decreasing exposure to ultraviolet radiation and the use of sunscreen[4].The paper provides and overview of contributory factors and treatment of non-melanoma skin cancers.

II. Contributory factors

Ultraviolet radiation from sun exposure is the primary environmental contributory factor(cause) of skin cancer[10].Other contributory factors includes:

a).Smoking tobacco[11]

b).HPV infections increase the risk of squamous –cell skin cancer[11]

c).Genetic syndromes, including congenital melanocystyic nevi syndrome which is characterized by the presence of nevi(birthmarks or moles) of varying size which are either present at birth or appear within 6 months of birth.Nevi larger than 20mm(3/4") in are at higher risk for becoming cancerous[11].

d).Chronic non-healing wounds. These are called Marjolin's ulcers based on their appearance, and develop into squamous cell cancer[11].
e).Ionizing radiation such as X-rays,environmentalcarcinogens,artificial UV radiation(e.g.tanning beds),aging and light skin color[11]It is believed that tanning beds are the cause of hundreds of thousands of basal and squamous –cell skin cancer[12].The World Health 0rganization now places people who use artificial tanning beds in its highest risk category for skin cancer[13].Alcohol consumption specifically excessive drinking increase risk of sunburns[14].
f).The use of many immunosuppressive medications increases the risk of skin cancer.Cyclosporin A, a calcineurin inhibitor for example increases the risk of approximately 200 times, and azathioprine about 60 times[15].

III. Pathognomonic

A malignant epithelial tumor that primarily originates in the epidermis, in squamous mucosa or in areas of squamous metaplasia is referred to as a squamous-cell carcinoma [16].

Macroscopically, the tumor is often elevated,fungating,or may be ulcerated with irregular borders. Microscopically, tumor cells destroy the basement membrane and sheets or compact masses which invade the subjacent connective tissue(dermis).In well differentiated carcinomas, tumor cells are pleomorphic/atypical but resembling normal keratinocytes from prickle layer(large,polygonal, with abundant eosinophilic(pink) cytoplasm and central nucleus[16].

Their disposal tends to be similar to that of normal epidermis immature/basal cells at periphery, becoming more mature to the Centre of the tumor masses. Tumor cells transform into keratinized squamous cells and form round nodules with concentric, laminated layers, called "cell nests" or "epithelial/keratinous pearls". The surrounding stroma is reduced and contains inflammatory infiltrate(lymphocytes).Poorly differentiated squamous cells and no keratinization[16].A molecular factor involved in the disease process is mutation in gene PTCHI that plays and important role in the Sonic hedgehog signaling pathways[17].

III. Clinical Manifestations

Basal- cell carcinoma (BCC)grows slowly and can damage the tissue around it but is unlikely to spread to distant areas or result in death [3].It often appears as a painless raised area of skin. That may be shiny with small vessel running over it or may present as a raised area as an ulcer[2].
Squamous-cell skin carcinoma (SCC) is more likely to spread [3].It usually presents as a hard lump with scaly top but may also form an ulcer [8].
Melanoma also known as malignant melanoma.Melanomas are most aggressive. Signs include a mole that has changed size,shape,color,has irregular edges, has more than one color,is itchy or bleeds[9].Most melanoma consist of various colors from shades of brown to black.A small number of melanoma are pink,red or fleshy in color, these are called amelanotic melanoma and tend to be more aggressive. Warning signs of malignant melanoma include change in size,shape,color or elevation pf a mole. Other signs are the appearance of new mole during adulthood or pain,itching, ulceration, redness around the site, or bleeding at site.
An often-used mnemonic is"ABCDE",where A is for "asymmetrical",B for "Borders"(irregular "Coast of Maine sign"),C for "color"(variegated), D for "diameter"(larger than 6 mm-size of pencil eraser) and E for "evolving" [18,19].
Non-melanoma skin cancer {NMSC): Approximately 2,000 people die from basal 0r squamous cell skin cancers (non-melanoma skin cancers) in the United States each year. The rate has dropped in recent years. Most of the deaths happen to people who are elderly and might not have seen a doctor until cancer had spread, and people with immune system disorders [20].Miscellaneous skin cancer include Merkel cell carcinomas are most often rapidly growing, on-tender red, purple or skin colored bumps that are not painful or itchy. They may be mistaken for a cyst or another type of cancer [21].

IV. Treatment

Treatment of skin cancer dependent on type of cancer, location of the cancer, age of the person, and weather the cancer is primary or recurrence. Treatment is also determined by the specific type of cancer. For a small basal-cell cancer in a young person; the treatment with best cure rate (Mohs surgery or CCPDMA) might be indicated. In the case of an elderly man with multiple complicating medical problems, a difficult to excise basal-call cancer of the nose might warrant radiation therapy (slightly lower cure rate} or no treatment at all. Topical chemotherapy may be indicated for a large basal-cell carcinoma for good cosmetic outcome whereas it might be inadequate for invasive or invasive squamous- cell carcinoma. In general, melanoma is poorly responsive to radiation or chemotherapy. For low- risk disease, radiation(external beam radiotherapy or brachytherapy),tropical chemotherapy(imiquimod or 5-fluorouracil) and cryotherapy(freezing the cancer off) can provide adequate control of the disease, all of them, however may have lower overall cure rates than certain

type of surgery. Other modalities of treatment such as photodynamic therapy, tropical chemotherapy, electrodessication and curettage can be found in the discussions of basal-cell carcinoma and squamous cell carcinoma {22],

Mohs' micrographic surgery (Mohs surgery) is a technique used to remove the cancer with least amount of surrounding tissue and edges are checked immediately to see if tumor is found. This provides the opportunity to remove the least amount of tissue and provide the best cosmetically favorable results. Thisespecially important for areas where excess skin is limited, such as face. Cure rates are equivalent to wide excision. Special training is required to perform this technique. An alternative method is CCPDMA and can be performed by a pathologist not familiar with Mohs surgery. In the case of the disease that has spread(metastasized),further surgical procedures or chemotherapy may be required[23].Treatments for metastatic melanoma include biologic immunotherapy agents ipilimumab,permbrolizumab,andnivolumab,BRAFinhibitors, such as vermurafeniband dabrafenib,anda MEK inhibitor trametinib[24].

Plastic or reconstruction surgery

Currently, surgical excision is the most common form of treatment for skin cancers. The goal of plastic surgery or reconstruction is to restoration of normal appearance and function. The choice of technique in reconstruction is dictated by the size and location of the defect. Excision and reconstruction of facial skin cancers is generally more challenging due to presence of highly visible and functional anatomic structures in the face. When skin defects are small in size, most can be repaired with simple where skin edges are approximated and closed with sutures. This will result in a linear scar. If the repair is made along a natural skin fold or wrinkle line, the scar will be hardly visible. Larger defects may require repair with a skin graft, local skin flap,pedicled skin flap, or a microvascular free flap. Skin grafts and local skin flaps are by more common than listed choices. Skin grafting is patching of a defect with skin that is removed from another site in the body. The skin graft is sutured to the edges of the defect, and bolster dressing is placed atop the graft for seven to 10 days, to immobilize the graft at it heals in place. There are two forms of skin grafting split thickness and full thickness. In a split thickness skin graft, a shaver is used to shave a layer of skin from the abdomen or thigh. The donor site regenerates skin and heals over a period of two weeks. In a full thickness skin graft, a segment of skin is totally removed and donor site to be sutured closed [25].

Split thickness grafts can be used to repair larger defects, but the grafts are inferior in their cosmetic appearance. Full thickness skin grafts are more acceptable cosmetically. However, full thickness grafts can only be used for small or moderate sized defects. Local skin flaps are a method of closing defects with tissue that closely matches the defect in color and quality. Skin from the periphery of the defect site is mobilized and positioned to fill the deficit. Various forms of local flaps can be designed to minimize cosmetic outcome of reconstruction. Pedicled skin flaps are method of transferring skin with an intact blood supply from a nearby region of the body. An example of such reconstruction is a pedicled forehead flap for repair of a large nasal defect. Once the flap develops a source of blood supply from its new bed, the vascular pedicle can be detached [26].

V. Disease outcome

Disease outcome or prognosis of skin cancer is different in three types of skin cancers. The mortality rate of basal-cell and squamous –cell carcinoma are around 0.3%, causing 2000 deaths per year in the US. In comparison, the mortality rate of melanoma is 15-20% and it causes 65000 deaths per year [27].Even though it is much less common, malignant melanoma is responsible for 75% of all skin cancer related deaths [28].

The survival rate for people with melanoma depends upon when they start treatment. The cure rate is very high when melanoma is detected in early stages, when it can easily be removed surgically. The prognosis is less favorable if melanoma has spread to other parts of the body[29].As of 2003 the overall five year cure rate with Mohs micrographic surgery was around 95 percent for recurrent basal-cell carcinoma[30].

Australia and New Zealand exhibit one of the highest rates of skin cancer incidence in the world, almost four times the rates registered in the United States, the UK and Canada. Around 434,000 people receive treatment for non-melanoma skin cancers and 10,300 treated for melanoma. Melanoma is the most common type of cancer in people between 15-44 years in both countries. The incidence of skin cancer has been increasing [31].The incidence of melanoma among Auckland residents of European descent in 1995 was 77.7 cases per 100,000 people per year and predicted to increase in the 21st century because of "the effect of local stratospheric ozone depletion and the time lag from sun exposure to melanoma development[32].

VI. Preventive measure

Sunscreen is effective and thus recommended to prevent melanoma[33],and squamous –cell carcinoma[34].There is little evidence that it is effective in preventing basal-cell carcinoma[35].Other advice to

reduce rates of skin cancer includes avoiding sunburning, wearing protective clothing, sunglasses and hats, andattempting to avoid sun exposure or period of peak exposure[36].The U.S. Preventive Services Task Force Recommends that people between 9 and 25 years of age be advised to avoid ultraviolet light[37].

The risk of developing skin cancer can be reduced through a number of measures including decreasing indoor tanning and mid-day sun exposure, increasing the use of sunscreen, and avoiding the use of tobacco products [37].There is insufficient evidence either for or against screening for skin cancers [38]. Vitamin supplements and antioxidant supplements have not been found to have an effect in prevention [39].Evidence for a benefit from dietary measures is tentative [40].

Zinc oxide and titanium oxide are often used in sun screen to provide broad protection from UVA and UVB ranges [41].Eating certain foods may decrease the risk of sunburns but this is much less than the protection provided by sunscreen [42].

VII. Conclusions

The majority of Non-melanoma skin cancers (NMSC) are basal-cell and squamous-cell cancers. Australia and New Zealand have highest rates of skin cancers in the world. The incidence of melanoma among Auckland of European descent was 77.7 cases per100,000peryear.Prevention by decreasing exposure to ultraviolet radiation and the use of sunscreen.

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