Introduction

Cancer of skin is one of the most common human malignancies ***(El Bolkainy et al., 2005).*** It is the most common form of cancer in the United States. More than one million skin cancers are diagnosed annually ***(American Cancer Society, 2008).*** One in five Americans will develop skin cancer in the course of a lifetime ***(Robinson, 2005).***

In many areas of the world, primary skin cancer is increasing ***(Soutar and Ropertson, 2002).***

In Egypt, the National Cancer Institute (NCI) provided the relative frequency of skin cancers during the five years period from 1985 to 1989.They reported that malignant tumors of the skin constitute 5.71% of total malignancies, with high adult predominance of 94.2% and male predominance of 67.98% ***(Mokhtar, 1991).***

Skin cancer is divided into Melanoma skin cancer (MSC) and Non melanoma skin cancer (NMSC) which includes: squamous cell carcinoma, basal cell carcinoma and adnexal tumors. Other NMSC includes: Dermatofibrosarcoma protuberans, Kaposi's sarcoma, Mycosis Fungoides and Merkle cell carcinoma ***(El Bolkainy et al., 2005)***.

American cancer society predicted that 1.3 million new cases of NMSC would occur in year 2003 ***(American Cancer Society, 2002).*** On the other hand, approximately 59,580 new

cases of malignant melanoma were predicted for the United States in 2005 ***(Jermal et al., 2005).***

Approximately 80% of skin cancers are basal cell carcinoma. It is the most common form of skin cancer; about one million of the cases diagnosed annually are BCCs ***(American Cancer Society, 2008).***

Squamous cell carcinoma (SCC)is the second most common form of skin cancer, it accounts for 16% of skin cancer, more than 250000 cases are diagnosed each year, resulting in approximately 2500 deaths ***(American Academy of Dermatol, 2008).***

The incidence of Melanoma is increasing faster than that of almost any other cancer ***(SEER, 2004)***. It accounts for only 4% of all skin cancers but for 75% of skin cancer deaths ***(American Cancer Society, 2002).***

El Bolkainy and colleagues (2005) added that NMSC shows a case fatality rate of only 0.2 % while MSC shows a case fatality rate of at least 20% **.**

Aim of the Work

The aim of this work is registration of primary malignant tumors of the skin received at the Pathology Department of Ain Shams University Hospitals and Ain Shams Specialized Hospitals during a period of 5 years (2001-2005), with registration of the available clinico- pathological data from the files.

In addition registration of the incidence of the total number of malignant tumors received during the same period will be reported.

Histological Structure of the Skin

The skin is the heaviest single organ of the body, accounting for about 16% of total body weight and in adults presenting 1.2-2.3m² of surface to the external environment. It is composed of the epidermis, an epithelial layer of ectodermal origin, this layer is differentiated to 5 layers of keratin producing cells (keratinocytes), these layers are stratum basalis, stratum spinosum, stratum granulosum, stratum lucidum and stratum corneum ***(Hentula et al., 2001).***

Following the epidermis is the dermis, a layer of connective tissue of mesodermal origin that binds the epidermis to the subcutaneous tissue (hypodermis). Based on the comparative epidermis, thick and thin skin can be Distinguished **(Figure 1).**

The junction of dermis and epidermis is irregular, and projections of the dermis called papillae interdigitate with invaginations of the epidermis known as epidermal rete ridges.

Epidermal derivatives include hairs, nails, sebaceous and sweat glands. Beneath the dermis lies the hypodermis or subcutaneous tissue, a loose connective tissue that may contain a

pad of adipose cells, the panniculus adipose. The hypodermis, which is not considered part of the skin, binds skin loosely to the subjacent tissues and corresponds to the superficial fascia of gross anatomy ***(Luiz and Jose, 2003).***

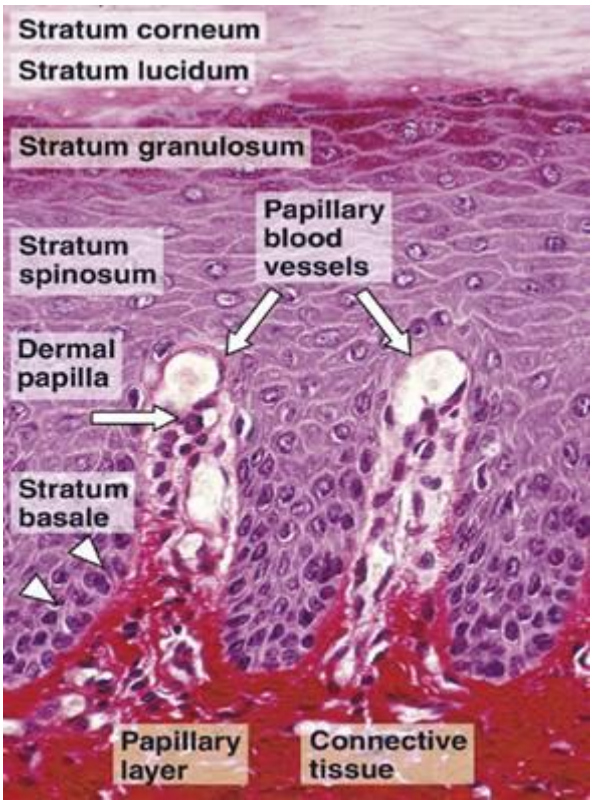

Figure (1): Phtomicrograph of thick skin *(Luiz and Jose, 2003).*

Classification of Primary Malignant Skin Tumours

Malignant skin tumours were classified as follow:

I. According to Rosai and Ackerman's Surgical Pathology 2004(Rosai et al.,2004)

A. Epidermis

1) Actinic keratosis
2) Bowen's disease
3) Squamous cell carcinoma
4) Basal cell carcinoma

B. Skin adnexa

1) Eccrine sweat glands
   a) Sweat gland carcinoma
   b) Extra mammary Paget's disease
2) Apocrine glands
   - Apocrine carcinoma
3) Sebaceous glands
   - Sebaceous carcinoma

C. Melanocytes

- Malignant melanoma

D. Neuroendocrine cells

- Merkel cell carcinoma
- Other neuroendocrine tumours

E. Dermis

1) Fibroblastic tumours and tumourlike conditions
2) Fibrohistiocytic tumours and tumourlike conditions
    a) Dermatofibrosarcoma protuberans
    b) Malignant fibrous histiocytoma
3) Smooth muscle tumours
    - Cutaneous leiomyosarcoma
4) Skeletal muscle tumours
    - Rhabdomyosarcoma
5) Peripheral nerve tumours
    - Malignant schwannoma
6) Vascular tumours and tumourlike conditions
    a) Kaposi's sarcoma
    b) Angiosarcoma
7) Lymphoid tumours and tumourlike conditions
    a) Mycosis fungoides and related peripheral T-cell lymphomas
    b) Lymphomatoid papulosis and anaplastic large cell lymphoma
    c) Other malignant lymphomas
    d) Leukaemia

II. <u>According to World Health Organization classification of skin tumours, 2006(LeBoit et al.,2006)</u>

1) Keratinocytic tumours

A. Basal cell carcinoma
B. Squamous cell carcinoma
C. Bowen's disease
D. Epidermal dysplasia
   - Actinic keratosis
   - Arsenical keratosis

2) Melanocytic tumours

Malignant melanoma

3) Appendageal tumours

A. Malignant tumours with apocrine and eccrine differentiation
   - Tubular carcinoma
   - Microcystic adnexal carcinoma
   - Malignant mixed tumour
   - Porocarcinoma
   - Spiradenocarcinoma
   - Hidradenocarcinoma
   - Mucinous carcinoma
   - Digital papillary carcinoma
   - Adenoid cystic carcinoma
   - Apocrine carcinoma
   - Paget's disease and extramammary Paget's disease

B. Malignant tumours with follicular differentiation
   - Pilomatrical carcinoma
   - Proliferating tricholemmal tumour

C. Malignant tumours with sebaceous differentiation
   - Sebaceous carcinoma

4) Haematolymphoid tumours

5) Soft tissue tumours

III. <u>According to *Weedon & Strutton (1999)*</u>

1) Malignant tumors of the epidermis

A. Epidermal dysplasia
   - Actinic keratosis
   - Actinic cheilitis
   - Arsenical keratosis
   - PUVA keratosis

B. Intraepidermal carcinomas
   - Bowen's disease
   - Erythroplasia of Qeuart
   - Intraepidermal epithelioma(Jadassohn)

C. Malignant tumors
   - Basal cell carcinoma
   - Nevoid basal cell carcinoma syndrome
   - Squamous cell carcinoma
   - Verrucous carcinoma
   - Adenosquamous carcinoma
   - Carcinosarcoma
   - Lymphoepithelioma-like carcinoma

2) Malignant tumors of cutaneous appendages

A. Tricholemmal (external sheath) tumors
   - Tricholemmal carcinoma

B. Tumors with matrical differentiation
   - Pilomatrix carcinoma

C. Sebaceous tumors
   - Sebaceous carcinoma

D. Tumors of modified apocrine glands
   - Adenocarcinoma of Moll's glands
   - Ceruminous adenocarcinoma
   - Adenocarcinoma of anogenital mammary-like glands

E. Eccrine tumors
   - Microcystic adnexal carcinoma
   - Eccrine carcinoma
   - Polymorphous sweat gland carcinoma
   - Adenoid cystic carcinoma
   - Mucinous carcinoma
   - Malignant chondroid syringoma
   - Malignant cylindroma
   - Malignant eccrine spiradenoma
   - Malignant eccrine poroma
   - Hidradenocarcinoma
   - Miscellaneous sweat gland carcinoma

3) Malignant melanoma

4) Malignant tumors of fibrous tissue

A. Fibrosarcoma
B. Fibromyxoid sarcoma
C. Fibrohistiocytic tumors
- Dermatofibrosarcoma protuberans
- Malignant fibrous histiocytoma

C. Presumptive synovial and tendon sheath tumors
- Epithelioid sarcoma

5) Malignant tumors of fat
- Liposarcoma

6) Malignant tumors of muscle and bone

A. Tumors of smooth muscles
- Leiomyosarcoma

B. Tumors of striated muscles
- Rhabdomyosarcoma
- Malignant rhabdoid tumor

C. Tumors of bone
- Osteosarcoma

7) Malignant neural and neuroendocrine tumors
- Malignant nerve sheath tumors
- Merkle cell carcinoma
- Peripheral neuroectodermal tumor(=malignant neuroepithelioma)

8) Malignant vascular tumors

A. Tumors with uncertain behaviour

- Kaposi's sarcoma

B. Borderline malignancy

- Endovascular papillary angioendothelioma of childhood
- Epithelioid haemangioendothelioma
- Retiform haemangioendothelioma

C. Malignant tumors

- Angiosarcoma
- Lymphangiosarcoma
- Malignant Glomus tumor(Glomangiosarcoma)

9) Cutaneous infiltrates (Lymphoid and leukemic)

Primary malignant tumours of the skin according to WHO classification (Le Boit et al., 2006)

1) Keratinocytic Tumours

These are group of lesions derived from the proliferation of epidermal and adnexal keratinocytes. These lesions may be malignant tumours with aggressive behavior and metastatic potential as seen with Squamous Cell Carcinoma, other lesions are benign as acanthoma. Included in the spectrum are the epidermal dysplasia as Actinic Keratosis, Arsenical Keratosis and PUVA Keratosis and intraepidermal carcinoma as Bowen's disease, and bowenoid papulosis ***(Heaphy and Ackerman, 2000; Lober et al., 2000; Ackerman, 2001).*** Keratinocytic tumours are important public health problem, despite their comparatively low mortality rate ***(Weinstock, 1997).***

Keratinocytic Tumours account for approximately 90% or more of all skin malignancies, 70% of which are Basal Cell Carcinoma (BCC) which exceeds squamous cell carcinoma in frequency by a factor of approximately 5-1. If solar Keratosis is regarded as squamous cell carcinoma, then the latter becomes the more common tumour ***(Brand and Ackerman, 2000).*** The incidence for lifetime risk for the development of skin cancer is 1 in 5 in the USA ***(Rigel et al., 1996).***

A. Basal Cell Carcinoma

Definition:

A group of malignant cutaneous tumours characterized by the presence of lobules, columns, bands, or cords of basaloid cells, "germenative cells".

Epidemiology:

Basal Cell Carcinoma (BCC) develops predominantly in sun-damaged skin in individuals who are fair skinned and prone to sunburn ***(Buttner et al., 1998).*** Although Basal Cell Carcinoma typically occurs in adults, the tumour also develops in children ***(Rahbari and Mehregan, 1982).*** Arsenic exposure and ionizing radiation may also induce Basal Cell Carcinoma ***(Guo et al., 2001)***. BCC is very frequent tumours particularly in light skinned individuals living in countries at low latitudes. Incidence of 2000 per 100000 populations has been reported in Queensland, Australia.

The rate of Basal Cell Carcinoma has increased in older age groups. Older men have a higher incidence of Basal Cell Carcinoma than women, but women have been found to outnumber men in younger age groups. The latter may be due to increased sun exposure in younger women in association with smoking ***(Boyd and King, 2002).***

Clinical Features:

Basal Cell Carcinoma appears as papule or nodule that can be eroded or ulcerated; or in superficial forms, it appears as erythematous patches resembling an area of dermatitis.

Pigmented Basal Cell Carcinoma may masquerade as melanoma, but can be distinguished by pearly appearance and dermatoscopy. The clinical capacity to differentiate some Basal Cell Carcinoma from squamous Cell Carcinoma or even Melanoma may be impossible without skin biopsy. Incomplete removal of basal cell carcinoma may result in delayed recurrences that may not be recognized for years,particularly if the tumour recurrence is deep or masked by skin grafts ***(Menzies et al., 2000).***

Genetics:

Several tumour suppressor genes and porto-oncogenes have been implicated in the pathogenesis of basal cell carcinomas, including the human homologs of the Drosophila genes patched (PTCH) and smoothened (SMOH), the TP53 tumor suppressor gene, and the RAS proto-oncogene family ***(Reifenberger et al., 2005).*** Patients with PTCH polymorphisms are at increased risk of developing the disease ***(Strange et al., 2004).***

Histopathology:

The multiple variants of Basal Cell Carcinoma are connected by the common feature of lobules, columns, bands and cords of basaloid cells (germenative cells) associated with scanty