Research Article

New horizon in the Management of Malignant Pigmented Skin Tumors

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Abstract
In Egypt, according to cancer pathology report obtained from national cancer institute NCI, Cairo University, malignant skin tumors constituted 4.76% of total malignancy. A total of 4061 skin material cases presented to the Pathology Department, NCI during 2000 till 2011**.** Malignant melanoma represents a significant and growing public health burden in the US and worldwide. It is estimated that 76, 380 cases were diagnosed as invasive malignant melanoma and at least 10130 patients died because of melanoma in the US at 2016. **Conclusion and Recommendations:** Patients presenting with suspicious pigmented lesion optimally should undergo an excisional biopsy. Treatment of primary melanoma is wide surgical excision with safety margin differs according several factors. If sentinel lymph is negative, regional lymph node is not indicated
Keywords: New horizon, malignant, skin tumors

Introduction
Pigmented skin cancers can be classified into two types mainly {Melanocytic, nonmelanocytic skin tuomors (NMSCS)}. Melanocytic cancer (malignant melanoma) is less common than other skin cancers but it is much more dangerous, it causes the majority (75%) of deaths related to skin cancers.

Melanoma is a neoplastic disorder produced by malignant transformation of the normal melanocyte. Melanocytes are cells responsible for the production of the pigment melanin. Melanoma usually arises from melanocytes at the dermal/epidermal junction. (Chen et al, 2013). The classic appearance of primary cutaneous melanoma is summarized by "ABCD" for asymmetry, border irregularity, color variation, and diameter greater than 6 mm.

Because melanomas arise from melanocytes, which contain the melanin-synthetic pathway, melanomas classically are distinguished by their pigmentation (Curtin et al., 2005) Exactly what causes melanoma is unknown but incidence of melanoma increases with male sex, age more than 60 years, chronic sun exposure, presence of melanoma susceptibility polymerphisms (CDKN2A,CDK4,MC1R) and family history (Siegel et al., 2016)

Biopsy of a suspicious skin lesion is necessary for an accurate diagnosis and for optimal staging. The correct way to perform such a biopsy is to make a full-thickness biopsy of the entire lesion, with a narrow (1 to 2 mm) margin of grossly normal skin (Pins et al, 2011). The primary treatment modality for cutaneous melanoma is wide surgical excision, lymph node dissection. After the diagnosis of melanoma has been histologically confirmed and the primary lesion has been adequately microstaged, a wider and frequently deeper excision is needed to ensure complete removal (Yonick et al, 2011).

Aim of the work
To review literature for the recent updates in malignant pigmented skin tumors and the new modalities in diagnosis and management of this category of tumors.

Epidemiology of pigmented malignant skin tumors
In Egypt, according to cancer pathology report obtained from national cancer institute NCI, Cairo University, malignant skin tumors constituted 4.76% of total malignancy. A total of 4061 skin material cases presented to the Pathology Department, NCI during 2000 till 2011 (Ibrahim et al., 2010).

Malignant melanoma represents a significant and growing public health burden in the US and worldwide. It is estimated that 76, 380 cases were diagnosed as invasive malignant melanoma and at least 10130 patients died because of melanoma in the US at 2016. (Siegel et al., 2016).

Diagnosis of melanoma

Suspicious lesions are characterised by asymmetry, border irregularities, colour heterogeneity, dynamics, (dynamics or evolution in colours, elevation or size) ('ABCD rule'). Today, many primary melanomas have a diameter of <5 mm. (Drummer et al., 2011. Bono et al., 2006).

Updates in management of melanoma

Treatment of primary melanoma:

Wide excision

Surgical excision is the primary treatment of melanoma. Several prospective randomized trials have been conducted in an effort to define optimal surgical margins for primary melanoma.

In an international prospective study carried out by WHO, 612 patients with primary melanomas not thicker than 2 mm were randomized to wide excision with 1 cm or >3 cm margins. At a median follow up of 90 month s, local recurrence LR, disease free survival DFS; overall survival OS rates were similar in both groups**.** (Veronesi, Cascinelli, 1991)

Treatment of stage III in transit disease

The tumor burden, time course of appearance, and duration of in-transit disease is variable. In some patients, In-transit lesions remain confined to a region of the body for many years. This may occur in isolation or in combination with other sites of metastatic disease. A major concern in patients in which in-transit disease occurs in isolation is the high probability of subsequent development of visceral metastasis.

Treatment for distant metastatic melanoma Stage IV

Systemic therapy for advanced melanoma:

The therapeutic landscape for metastatic melanoma is rapidly changing with the recent development of novel agents, which have demonstrated better efficacy than traditional chemotherapy. The first generation of novel targeted and immunotherapy (vemurafenib, dabrafenib, ipilimumab) demonstrated significantly improved response rates and outcomes compared with conventional therapies. Subsequently, a number of ongoing or recently completed phase 2 and phase 3 trails testing new immunotherapy drugs and targeted therapies and combination regimens have yielded noteworthy results. A second generation of effective agents and combination regimens are now available for treatment of advanced unresectable or metastatic melanoma (Weber et al., 2015)

Recurrence

Patterns of recurrence

Stage specific probability of recurrence: the likelihood of recurrence is dependent on the stage of the primary disease at presentation .with increasing stage at first presentation, risk of recurrence increases and the distribution of recurrences changes. (Romano et al., 20 10)

Recurrence rates for completely excised melanoma in situ are sufficiently low that patients are considered cured following excision, with the exception that certain subtypes may recur locally (lentigo maligna) (Duffr et al., 2014)

For patients who present with stage 1-2 melanoma and and who are rendered free of disease after initial treatment, recurrences are distributed as follows: approximately 15% to 20% are local or in-transit, 50% in regional lymph nodes and 29% at distant metastatic sites**.** (Soong et al., 1998)

Pigmented nonmelanocytic skin cancers

1- Pigmented basal cell carcinoma (BCC):

Pigmented basal cell carcinoma arises from the basal cells present in the lower layer of the epidermis. It is the most common over exposed areas of skin in direct proportion to the number of pilo sebaceous units present in that area. It is a slow growing tumor that rarely metastasizes but can cause extensive destruction of the surrounding tissue and bone, referred to as rodent ulcer.Clinicians must be aware of the variants of BCC to avoid errors in diagnosis and management, it rarely mimics melanomas when pigmented (Patterson et al., 2006)

Conclusion and Recommendations

Patients presenting with suspicious pigmented lesion optimally should undergo an excisional biopsy.

Treatment of primary melanoma is wide surgical excision with safety margin differs according several factors.
If sentinel lymph is negative, regional lymph node is not indicated.

Patients presenting with clinically positive lymph nodes without radiological evidence of distant metastases should undergo wide surgical excision of the primary site and complete lymph node dissection.

Therapies for isolated in transit disease include local, regional, and systemic therapy, the choice of therapy depends on the health status of patients and tumor burden.
For patients with of unresectable or metastatic melanoma, recommended treatment options include checkpoint immunotherapy, BRAF targeted therapy and palliative radiotherapy.

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