Skin Cancer: Basal Cell Cancer (BCC) and Melanoma (Malignant Melanoma)

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Neoplasms of the skin can be hard to differentiate clinically, but nevertheless they can result in entirely different consequences. While the colloquially called “white skin cancer” describes rather harmless changes of the skin, the “black skin” cancer is feared. As other doctors from different specialties, other than dermatologist, are also consulted when discussing diagnostic findings of their patients’ skins, it pays off to know the most common types of skin cancer.

Basal-Cell Carcinoma – Aggressive and Local
Basalioma or basal-cell carcinoma is the most common neoplasm of the skin. It is nonmelanoma skin cancer (NMSC). It forms the novo emanating from basal cells, which means it is not based on a precancerous condition. Basaliomas solely affect haired skin and usually appear in areas that are exposed to sunlight (Ultraviolet radiation from sun). The most common localization is the face, head and neck: about 80 % of all basaliomas appear on the connecting line between the corner of the mouth and the earlobe.

**Risk Factors of Basalioma**

1. Mutations, which are evoked by years or decades of chronic UV-exposure, are causal for the formation of basaliomas and people having brighter skin color are particularly threatened.
2. Apart from mutagenesis that leads to DNA damage excessive exposure to sunlight depress the immune system.
3. Arsenic-exposure may as well lead to malignant degeneration of basal cells.
4. Exposure to radiations (X-rays)

**Characteristics of Basalioma**

- Basalioma almost never metastasizes
- However, it destructs and grows locally, and is able to induce significant damage to the surrounding tissue.
- Sun exposure is most common cause of basalioma, however body areas not exposed to sun are considered to have genetic susceptibility for basalioma
- They appear as pearly translucently to fleshy color raised area of skin, raised area may contain tiny blood vessels (telangiectasia) and sometimes characterized by ulcers (Image 1).
- In large Basalioma bleeding, oozing and crusting frequently develops.

**Types of Basalioma**
Encountering morphologic features, there are various types of the basalioma

1. **Nodular basalioma (Image 2):** It is characterized by a single or multiple central nodules having a string-of-pearls margin and telangiectasias (small dilated blood vessels).

2. **Superficial:** It appears due to superficial proliferation of neoplastic basal cell

3. **Infiltrative basal cell carcinoma:** In this tumor penetrate into dermis in thin strands between collagen fibers.

**Diagnosis and treatment**

**Basal-cell carcinomas** are curable and can be treated with topical medications, surgery or various therapies such as:

1. **Surgical excision:** Gold standard in therapy, subsequent to clinical and histological confirmation of the diagnosis, is the **surgical excision** of the tumor. Adequate safety margins are obtained and a successive histological follow-up of the cutting edges is performed. In areas where extensive excision is impossible due to aesthetic reasons (i.e. the face) the tumor should be excised under constant intraoperative examination of the margins of resection (so-called **micrographic controlled excision**). Mohs micrographic surgery is used for tumors that are difficult to excise.

2. Superficial tumors alternatively may be treated with **cryotherapy**, **photodynamic therapy or local chemotherapy**. In cases of inoperable basalomas **radiotherapy** is the treatment of choice. Furthermore, hedgehog-inhibitors were admitted in 2013 as alternative treatments for non-resectable basaliomas. Patient with hedgehog inhibitors are often treated with arsenic trioxide and itraconazole.
3. Radiation therapy is used for old age patients and topical fluorouracils are used treatment of superficial BCC.

After curative therapy has taken place, periodic (yearly) follow-ups are suggested, since there is a high risk of developing further primary tumors.

**Notes regarding basalioma:**

- Almost no metastasis, local infiltration of the surrounding tissue
- The face is the most common localization.
- String-of-pearls margin and telangiectasias
- Micrographic controlled surgery is the therapy of choice, yearly check-ups

**Malignant Melanoma – Silent and Spreading**

Not the most common, but the most feared type of skin cancer involves **malignant degeneration of melanocytes** – the malignant melanoma. It **accounts for over 90 % of deaths caused by skin cancer**. Chronic UV-light exposure, damages caused by sunlight including sunburns (especially during childhood and adolescence), bright (Celtic) skin type and cumulative appearance of melanocytic nevi (> 100) or the presence of dysplastic nevi represent significant risk factors. The most important risk factor is exposure to sunlight, particularly UV-B radiation.

**Risk factors**

1. **Cutaneous melanomas** of the head and neck are significantly more likely to occur in people with high levels of total sun exposure. Conversely, melanomas on the trunk tend to develop on people with lower levels of ambient sunlight exposure, but who also experience higher levels of recreational exposure on the chest and back.
2. Changing mole is considered as most important clinical risk factor associated with cutaneous melanoma
3. Age: Sunburns early in life, age older than 50 and exposure to UV radiation from tanning beds are other factors in the development of melanoma.
4. Fair skin phenotype: People who burn easily, such as those with fair or red hair, blue eyes, and light-colored skin, are most prone to develop melanoma.
5. Nevi: The presence of freckling and benign nevi also indicates an increased risk for melanoma development. The number of nevi appears to be more important than the size. The presence of more than 100 benign-appearing nevi in adults or greater than 50 clinically normal nevi in children increases risk. Additionally, a patient with any atypical or dysplastic nevi is at a heightened risk.
6. Presence of xeroderma pigmentosum or familial atypical mole melanoma syndrome.
7. Previous melanoma: Patients with a previously diagnosed melanoma are also at increased risk, and 5-10% eventually develop a second primary.
8. Gender difference: A noticeable fact is that women are more likely get affected on their upper thighs, whereas men tend to get malignant melanoma on their upper body.

Note: Malignant melanoma, unlike basalioma, appears **often on areas of the body that are not exposed to sun light**.

Considering morphological and histological aspects, there are **4 types** of malignant melanoma: The most common type is the
- **Superficial spreading melanoma** (60 %), which first grows in width and later on in depth. Lesions are flat and irregular in shape.
- **Nodular melanoma** (20 %) impresses with its nodular growth and primarily tends to grow in depth, which is why it has a worse prognosis.
- **Lentigo maligna melanoma** (10 %) is a common melanoma found in old people. Its causal reason is hyperpigmentation (lentigo senilis) and they tend to present widespread and initially grow horizontally before growing in thickness (good prognosis). Lesions large, flat and brownish.
- **Acral lentiginous melanomas** (5 %) also grow horizontally at first and are usually found in the area of the palm of the hand, the soles of feet or around the affected person’s fingernails. The Hutchinson’s sign, which refers to a spread onto the periungual skin, is a characteristic clinical sign.

**Diagnosis-ABCDE-mnemonic**

Metastasis of the malignant melanoma is either **effected by lymphatic or by hematogenous spread**. As a consequence of loco-regional spread, metastases can appear on the patient’s skin (satellite metastases). The liver, skeleton and brain are among other locations where distant metastases are commonly found.

The **ABCDE-mnemonic** is a popular method for early detection of melanomas. Nevi which meet one or more of the following criterions should undergo further evaluation using a reflected-light microscope (dermatoscopy).

- A (asymmetry) = asymmetrical shape
- B (border) = irregular margin and indistinct border
- C (color) = varying pigmentation
- D (diameter) = above 5 mm
- E (elevated, enlarging) = convexness and rapid increase in size

If a dermatoscopy confirms a primary tumor, a complete surgical excision with adequate surgical margins (0,5cm) is performed whereupon the excisional skin undergoes a subsequent histopathological examination. In case of histological confirmation of a malignant tumor, skin margins must be resected depending on the tumor’s thickness (see below) and depth of tumor invasion: A melanoma-in-situ (tumor does not penetrate the basal lamina) has to be removed including a safety margin of 0,5 cm (so no resection is necessary). For a melanoma that has grown across the basal lamina, the following safety margins apply (according to the S3-guideline):

- tumor thickness < 1-2 mm: 1 cm
- tumor thickness > 2 mm to 4 mm: 2 cm

**Note:** **Breslow’s depth** is defined as the histologically determined depth of infiltration in mm, starting from the granular layer of the epidermis. It is a determining criterion for the prognosis of the melanoma and defines the T-stage of TNM-classification.

After histological analysis of a malignant melanoma is completed, **clinical staging** should follow, whose extent is determined by histopathological findings. It includes the search for lymph node metastases using lymph node sonography, a chest X-ray in two planes, an abdominal sonography and a skeletal scintigraphy. For the exclusion of distant metastases a whole-body CT and MRI should be considered.

**Treatment**

Therapy of choice for malignant melanoma is **surgical excision**. Adjuvant therapy does not yield higher survival rates. However, patients in progressed tumor stages may benefit
from adjuvant immunotherapy using \textit{interferon-alpha.}

Present metastases are to be treated using adequate methods (i.e. \textit{surgical resection, radiotherapy}).

**Immunotherapy:** The latest \textbf{greatest innovation in the therapy of melanoma} is \textbf{immunomodulation}. The monoclonal antibody Ipilimumab has been accredited since 2011. Ipilimumab reinforces the body’s own immune reaction against tumor cells by blocking their receptors, which induces a down-regulation of the immune response. This way, a tolerance, which the body establishes against the growing tumor cells, is impaired. A similar mechanism is used by the PD1-inhibitor Nivulomab. According to current data (ongoing trials), the combination of Nivolumab and Ipilimumab seems to be promising, but also shows significant side effects.

**Notes regarding melanoma:**
- Early lymphogeneous spreading
- Most commonly located on women’s thighs or on men’s torsos.
- ABCDE-mnemonic helps in early recognition.
- T-stage is defined by Breslow’s depth.
- Excision is therapy of choice, safety margin depends on the tumor’s depth.

**References**


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