Figure 8.25: Marjolin's ulcer developed over chronic post burn contractures of the foot

A notable variant is **Marjolin's** ulcer, a highly aggressive malignant tumor that develops in areas of chronic ulceration (e.g., pressure ulcers, fistulas, or burn scars), with an increased potential for metastasis (Fig. 8.25).

Verrucous carcinoma is characterized by a verrucous papillomatous lesion that invades deeply into the dermis. Generally well-differentiated with low metastatic potential, this variant includes lesions like giant condylomata acuminatum (GCA), also known as Buschke-Lowenstein tumor (Fig. 8.26), and epithelioma cuniculatum, which may transform into verrucous carcinoma. Management is surgical, similar to that of SCC.

Precancerous lesions

The most common precursor to SCC is *actinic (solar) keratosis*, which appears as a well-defined, scaly, maculopapular lesion with a rough texture on sun-damaged skin

Figure 8.26: Verrucous carcinoma developed over giant condylomata acuminatum

(Fig. 8.27). Due to its potential to progress to SCC, treatment often involves electrocautery, liquid nitrogen, or 5-fluorouracil (5-FU).

Leukoplakia, a common precancerous lesion of the oral mucosa, is often associated with smoking and poor oral hygiene and appears as whitish patches that may progress to SCC if untreated.

Bowen's disease is an in situ form of

Figure 8.27: Facial actinic keratoses

Figure 8.28: Bowen's disease

SCC typically presenting as a slow-growing erythematous plaque with irregular borders (Fig. 8.28). Early diagnosis and surgical treatment offer the best prognosis.

Erythroplasia of Queyrat presents as a shiny red plaque on the glans penis, oral mucosa, or vaginal mucosa, with a 30% risk for malignant transformation.

Treatment

SCC treatment resembles that of BCC, with wide **surgical excision** and immediate defect reconstruction being the most definitive approach. Safe resection margins are 4-6 mm for low-risk and 10 mm for high-risk lesions. Mohs micrographic surgery offers 95% cure rates for primary tumors, and has similar indications and limitations, as for BCC.

Lymphadenectomy is indicated for clinically palpable lymph nodes. Radiation therapy is generally reserved for patients who cannot undergo surgery or for high-grade tumors, typically as an adjunctive treatment following surgical excision.

Chemotherapy is usually reserved as adjuvant treatment for advanced or recurrent tumors, and metastatic disease.

Postoperative follow-up

Close postoperative monitoring is essential for detecting local recurrence or metastasis, particularly with regional lymph node assessment. Low-risk patients benefit from semiannual follow-ups for three years, while high-risk patients require clinical exams and ultrasound monitoring of lymph nodes every three months for the first two years, followed by semiannual exams for life. Patients are educated about sun protection and encouraged to self-examine the surgical site regularly.

Melanoma

Melanoma, although representing only 1.2% of all skin cancers, is the most rapidly increasing form of skin cancer worldwide, with a global incidence rise of 4-7%. It is highly malignant and associated with elevated mortality rates.

Epidemiology

In the U.S., melanoma incidence has more than tripled over the past 20 years. From 2012 to 2023, annual cases of invasive melanoma increased by 27%. The estimated annual healthcare cost of melanoma treatment now exceeds $930 million. The average age at diagnosis is 55, with a higher prevalence in men. Globally, the highest incidence rates occur in Australia and New Zealand, while the lowest are in China and Japan.

Predisposing Factors

Several factors increase the risk of developing melanoma:

- Phenotype: Individuals with lighter skin are at greater risk.
- Race: Incidence rates are 10-20 times higher in whites compared to people of color.
- Ultra-violet (UV) exposure: A history of severe sunburns, particularly in childhood, increases the risk.
- Multiple pigmented moles: Having more than 25 common moles is a risk factor.
- Atypical or dysplastic moles: The pres-

Figure 8.29: Typical melanoma of the back

Figure 8.30: Melanoma of the leg, in a female patient

ence of atypical moles also elevates risk.
- Family history: Approximately 10% of melanoma patients report a family history of melanoma.

Pathophysiology

Melanoma originates from melanocytes in the basal epidermal layer. These melanocytes produce melanin in response to sunlight, transferring it to keratinocytes to protect the cell nuclei from UV radiation. Normally, keratinocytes regulate melanocyte growth, but this balance is disrupted in melanoma. Intermittent, intense sun exposure is more damaging than consistent exposure due to the risk of cellular mutations before melanin production can adapt to protect the skin.

Clinical Presentation

Melanoma primarily affects the skin, but it can also develop in mucous membranes (e.g., gastrointestinal tract, genitals, eyes) and meninges. In men, melanomas commonly occur on the trunk and head (Fig. 8.29), while in women, they are more frequent on the lower extremities (Fig. 8.30). Facial melanomas often affect older adults and typically arise from lentigo maligna.

The ABCDE criteria (Fig. 8.31) help in melanoma diagnosis:

- **A**symmetry: Uneven halves of the lesion
- **B**order irregularity: Jagged, uneven borders
- **C**olor variation: Multiple colors within the lesion
- **D**iameter: Larger than 6mm
- **E**levation: Raised area with a palpable nodule

Melanoma growth patterns

Melanomas can exhibit various growth patterns, each with unique characteristics:

- ***Superficial spreading melanoma***
  It is the most common type, accounting for 50-70% of melanomas, typically developing radially on a *preexisting dysplastic mole*. It features asymmetrical borders, an average diameter of about 2 cm, and prominent color variation (Fig. 8.32).

Figure 8.31: Dermatoscopy of a melanoma depicting the ABCDE criteria

Figure 8.32: Superficial spreading melanoma

Figure 8.34: Lentigo maligna of the face

- ***Nodular melanoma***
  This aggressive form is the second most common (15-30%), with a 2:1 male-to-female ratio.
  It typically appears as a *new lesion (de novo)* on healthy skin, showing vertical growth and presenting as a dark-colored nodule with smooth borders that may ulcerate and bleed (Fig. 8.33).
- ***Lentigo maligna***
  This rare subtype (5%) has the least aggressive behavior, commonly affecting *older adults* (65-70 years) and predominantly women. It typically develops in chronically sun-exposed areas, such as the face and neck, starting as a non-palpable, irregularly bordered lesion confined to the epidermis. Upon entering the dermal layer, it thickens and forms nodules (Fig. 8.34).
- ***Acral lentiginous melanoma***
  It is the rarest subtype (<5% of all melanomas), more common in women. It presents as dark brown or black lesions on the palms (Fig. 8.35), soles of feet, or under the nails *(subungual melanoma)*. A common sign is *Hutchinson's sign*, which describes periungual pigmentation of the nail fold and hyponychium (Fig. 8.36).
- ***Amelanotic melanoma***
  This rare but aggressive subtype presents as a non-pigmented lesion. Diagnosis is based on immunohistochemical staining.

Figure 8.33: Nodular melanoma

Figure 8.35: Palm melanoma

Figure 8.36: Periungual pigmentation (Hutchinson's sign) of a subungual melanoma

Staging

Melanoma staging uses a classification system based on various prognostic factors to guide treatment and prognosis. According to the 2018 guidelines of the American Joint Committee on Cancer (AJCC), melanoma staging follows the TNM classification, which evaluates the primary tumor (T), regional lymph nodes (N), and distant metastasis (M).

Factors such as lesion thickness, presence of ulceration, and mitotic rate are considered when assessing the primary tumor. The ***Breslow thickness is the most reliable prognostic factor*** and defines four stages:

- **T1:** < 1.00 mm
- **T2:** 1.01–2.0 mm
- **T3:** 2.01–4.0 mm
- **T4:** > 4.0 mm

Historically, ***Clark staging*** was also used, based on the anatomical depth of invasion and defining five levels:

- **Level I:** Lesion confined to the epidermis (in situ)
- **Level II:** Tumor invades the papillary dermis
- **Level III:** Tumor reaches but does not invade the reticular dermis
- **Level IV:** Tumor invades the reticular dermis
- **Level V:** Tumor extends to subcutaneous fat.

Recent studies suggest that Breslow thickness is a more reliable predictor of survival than Clark levels. Surgical excision margins and sentinel lymph node biopsy also depend on melanoma Breslow thickness.

The presence of lymph node involvement is another strong prognostic factor. If lymph nodes are not involved, the primary indicators are Breslow thickness and ulceration. Multiple involved lymph nodes or distant metastasis significantly reduces survival and worsens prognosis.

Diagnosis

Any pigmented skin lesion exhibiting asymmetry, irregular borders, color variation, diameter increase, ulceration, or rapid changes should be excised and biopsied. Suspicious lesions should be surgically excised rather than cauterized, allowing for complete histological examination.

For *excisional biopsies*, margins should be 2–3 mm. For large lesions (>1.5 cm) or lesions in areas where excising large skin surfaces is difficult, an incisional biopsy may be considered. If melanoma is diagnosed via incisional biopsy, further management should not rely on Breslow staging, as thickness may vary in unsampled areas. The biopsy should reach the underlying normal subcutaneous fat.

Surgical Treatment

Upon melanoma diagnosis, wide surgical excision of the lesion area should be performed as soon as possible. The excision margin depends on the tumor's Breslow thickness:

- ***In situ tumors:*** Excision margin of 0.5 cm
- ***Tumors <1 mm thickness:*** Excision margin of 1 cm
- ***Tumors 1–4 mm thickness:*** Excision margin of 2 cm
- ***Tumors >4 mm thickness:*** Excision margin of 2 cm

For subungual melanomas, amputation at the level of the proximal interphalangeal joint is recommended in locally advanced cases.

Lymph node surgery

For edium-thickness tumors (1–4 mm), a ***sentinel lymph node biopsy (SLNB)*** is performed alongside wide excision, using lymphoscintigraphy with radioactive technetium-99 (Tc 99). Lymphatic mapping relies on the theory that melanoma spreads through the lymphatic system, with one lymph node *(sentinel lymph node)* being the first to receive metastatic cells. If the sentinel node is disease-free, the entire node group is assumed to be metastasis-free. A positive sentinel node warrants targeted treatment and monitoring of the lymph node group; therapeutic lymph node dissection is performed if metastases are detected, if more than two sentinel lymph nodes are positive, or if extracapsular spread is present. Detecting lymph node involvement aids in staging, prognosis, and determining the need for additional therapy.

Indications for SLNB include:

- Tumor thickness ≥ 0.8 mm
- Tumor thickness ≤ 0.8 mm with Clark level IV or higher, regression, ulceration, ≥2 mitoses in the invasive portion, or young age
- Tumor of unknown thickness

Prior to SLNB, staging with MRI, CT, or PET is essential to detect possible distant metastases.

Adjuvant therapy

Once the tumor size, lymph node involvement, or distant metastases are evaluated, TNM staging is determined. In 2018, the AJCC established the following melanoma stages:

- **Stages I & II:** Localized disease
- **Stage III:** Lymph node involvement
- **Stage IV:** Distant metastasis

While chemotherapy agents have been used in adjuvant treatment, *immunotherapy* and *targeted therapy* have shown improved overall survival rates. Other therapies, such as interleukin-2, vaccines, and gene therapy, are still under investigation. Chemotherapy with dacarbazine (DTIC) shows a 10–20% response rate.

Isolated limb perfusion with cytotoxic agents (e.g., melphalan, actinomycin-D) has been used for over 30 years in limb melanoma cases and may improve 5-year survival rates compared to simple excision, particularly for local disease recurrence. *Electrochemotherapy* is also effective for extensive skin metastases.

Postoperative Monitoring

All melanoma patients require regular follow-ups. Asymptomatic patients should be monitored every 3 months for the first 2 years, every 6 months for the next 3 years, and annually thereafter.

For patients with small tumors (<1 mm thickness), regular monitoring should include liver function tests and lactate dehydrogenase (LDH) levels, along with chest X-rays. Patients with thicker tumors (Stages III-IV) require more frequent postoperative imaging, such as chest CT, abdominal ultrasound, PET scans, brain and neck MRI, for long-term surveillance. Retrospective studies suggest that most recurrences are detected through detailed patient history and clinical examination, rather than imaging alone. Due to the complexity, unpredictable behavior, and high mortality associated with melanoma, it is critical that patients receive ongoing management and follow-up from a multidisciplinary team of specialists in dedicated centers.

Figure 8.37: Dermatofibrosarcoma protuberans on the proximal thigh

Other Malignant Tumors of Skin and Soft Tissues

Other malignant skin and soft tissue tumors include:

- **Merkel cell carcinoma:** It is a rare skin tumor that appears as a flesh-colored nodule, typically on the face, head, and neck. Most often it develops in older individuals with a weak immune system. It is a highly aggressive tumor with a poor prognosis.
- **Dermatofibrosarcoma protuberans:** It is a low-grade tumor that develops slowly and presents with multiple nodules, clinically resembling a keloid. It typically affects the trunk and proximal extremities (Fig. 8.37). Wide surgical excision is recommended due to high local recurrence rates.
- **Soft tissue sarcomas:** These tumors originate from mesenchymal tissues and are named based on their origin (e.g., fibrosarcoma, liposarcoma, angiosarcoma, rhabdomyosarcoma). They present as solid, slow-growing masses in deep issues. Diagnosis requires MRI imaging with biopsy confirmation (Fig. 8.38). Treatment typically involves wide surgical excision, radiation, and chemotherapy, with prognosis largely determined by tumor size, degree of differentiation, and presence of metastasis.
- **Skin appendage cancers**

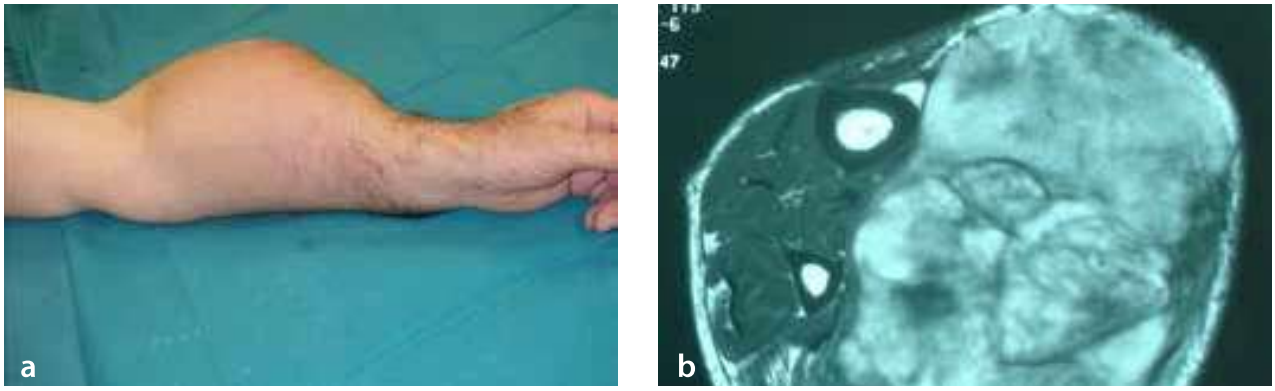

Figure 8.38: Large sarcoma of the forearm (a) and MRI imaging (b)

KEY POINTS TO REMEMBER
• A ganglion is the most common benign tumor of the hand.
• Seborrheic keratoses are common superficial brownish skin lesions, developing on the face, hands, and trunk; they can mimic melanoma.
• BCC is the most common skin malignancy, followed by SCC and malignant melanoma.
• BCC spreads slowly in the surrounding tissues with a very low risk of metastasis.
• SCC often spreads through lymphatic to regional lymph nodes; therefore lymph node examination is critical.
• SCC key prognostic factors include tumor size, location, and degree of cellular differentiation
• Sun exposure is a significant risk factor for all skin cancers.
• The standard treatment for skin malignancies is surgical excision with healthy margins while preserving function and cosmesis.
• Risk factors for melanoma include light skin, race (10-20 times higher in whites), severe sunburns, numerous or atypical moles, and family history. Pigmented lesions larger than 6-10mm in diameter are more likely to be malignant than benign.
• In melanoma, common sites include the trunk in men, the legs in women, and the face in older adults.
• The ABCDE criteria to evaluate skin lesions are Asymmetry, Border irregularity, Color variation, Diameter >6 mm, Elevation.
• Initial excision biopsy followed by wide local excision and sentinel node biopsy is the standard of care for melanoma.
• Breslow thickness is the most important prognostic factor for melanoma; excision margins are based on Breslow thickness.

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