Melanoma

Background

Melanoma is a malignant tumor, typically of the skin, that is associated with significant morbidity and mortality. Melanomas often begin as small, harmless-looking lesions with irregular borders, which progress to irregularly hyperpigmented asymmetric papules, nodules, or plaques with or without ulceration. If not treated promptly, metastasis is likely. Survival rates are contingent on the stage of the disease at the time of diagnosis and treatment (Swetter et al., 2019); education and early detection are critical to improving outcomes.

Assessment (Swetter & Geller, 2023)

Assess for risk factors:

- First or second-degree relative with a history of melanoma
- Light brown, blond, or red hair
- Light eye color (blue or green)
- High freckle density (greater than 50 common nevi)
- Fair skin type, light complexion
- Weakened immune system (e.g., solid organ transplant, HIV/AIDS patients)

Key questions to ask patients presenting with a lesion that is of concern:

- When was the lesion (or a change in a pre-existing lesion) first noticed?
- Has the lesion changed over time in size, shape, color, and/or symptoms (e.g., bleeding, itch)?
- Does the patient have a personal or family history of melanoma or other skin cancers?
- Does the patient have a history of excessive sun exposure and/or tanning bed use?
- Did the patient suffer severe sunburn during their childhood or teenage years?
- Does the patient have a cancer-prone syndrome (e.g., familial atypical mole and melanoma syndrome or xeroderma pigmentosum)?
- Is the patient immunosuppressed?

ABCDEs of assessment

Perform a total body skin assessment, including the palpation of regional and distant lymph nodes. A mole exhibiting any of the following signs should be referred for further examination and/or biopsy (Swetter & Geller, 2023):

- Asymmetry: if a lesion is cut in half, one side is not identical to the other; may be higher on one side, a different texture or color
- Border irregularity and bleeding: jagged edges, tails, bleeding, or ulceration are signs of melanoma
- Color variegation: 2 or 3 colors present or distributed unevenly
- Diameter: greater than or equal to 6 mm
- Evolving: any change in mole over weeks to months in size, shape, or color

“Ugly Duckling”: When a single lesion does not match the patient’s nevus (mole) phenotype or pattern (e.g., has a different appearance to surrounding moles).

In addition to the characteristics above, assess for any new skin lesion that is pigmented or vascular in appearance or any new pigmented line in a nail or lesion growing under a nail.

Documentation

- Number each mole, including location, size, and appearance.
- Document the presence of pain or itching in or around moles and lesions.
- When possible, photograph suspicious lesions.

Melanoma Subtypes (Swetter & Geller, 2023)

- **Superficial spreading melanoma (SSM)**
  - Most common type, accounting for 70% of all melanomas
  - Asymptomatic at first; thin, flat (1 mm or less in thickness), or slightly raised, with varying colors such as tan, brown, black, red, blue, gray, or white and irregular borders, ranging from a few millimeters to several centimeters in diameter
  - Confined to the epidermis, slow-growing and curable by surgical excision
- **Nodular melanoma (NM)**
  - Second most common type, accounting for 15 to 30% of all melanomas
  - Can develop on any area of the body, common on the head, neck, and trunk
  - Usually develops de novo as rapidly growing, darkly pigmented blue, black, pink, or red nodules that may ulcerate or bleed (late sign of invasive melanoma)
  - Assess for elevation, firmness, and continuous growth for one month
  - Associated with a poor prognosis
- Other subtypes of melanoma include:
  - **Lentigo maligna melanoma (LMM)**: accounts for 10 to 15% of all melanomas and develops in chronically sun-exposed areas (e.g., head and neck) and begins as large, tan, or brown pigmented macule that is flat or slightly raised with irregular borders
  - **Acral lentiginous melanoma (ALM)**: account for less than 5% of all melanomas but common in darker pigmented individuals; often found on acral sites (e.g., palms, soles, or beneath the nail) and appear as dark brown to black asymmetric macules with irregular borders and raised areas, ulceration, bleeding; may also present as benign lesions (e.g., warts, calluses, tinea pedis, nonhealing ulcers or ingrown toenails)
  - **Amelanotic melanoma**: pink or red macules, plaques, or nodules with well-defined borders; often mistaken with benign lesions
  - **Subungal (nail) melanoma**: longitudinal brown or black band on the nail (typically great toe or thumb) with or without nail dystrophy; common in advanced age, African Americans, Asians, and Native Americans

There are three rare subtypes of melanoma, including Spitzoid melanoma (resemble Spitz tumors), desmoplastic melanoma (appears as a scar or benign condition), and pigment synthesizing melanoma (melanocytoma).

Diagnosis (Swetter & Geller, 2023)

Dermoscopy

Dermoscopic examination can be performed on suspicious, pigmented lesions as a first-line diagnostic and may reduce the number of unnecessary biopsies. A dermoscope is a handheld light magnifier (10-fold magnification) used to assess the general appearance, pigmentation pattern, color, globules, dots, depigmentation, and margins. Proper training is necessary to use this specialized instrument that helps distinguish benign and malignant pigmented lesions.

Biopsy

All suspicious lesions should be biopsied for a definitive diagnosis.

- **Excisional/complete biopsy**: preferred biopsy technique with removal of entire growth with a margin of normal surrounding skin (1- to 3-mm margins), to a depth below the plane of the lesion; should be performed whenever possible; includes full-thickness elliptical, punch excision and deep shave removal ("scoop" biopsy)
- **Incisional biopsy** (partial sampling) or core biopsy: removes only a sample of the lesion; acceptable in select cases (e.g., face, palm, sole, ear, distal digit, subungual lesions, or very large lesions)
- **Fine-needle aspiration biopsy**: removes a small sample of tissue; not performed on a suspicious mole, but on deeper tissue (e.g., lymph node or internal organ) to check for metastasis
- **Narrow-margin excisional biopsy**: may be performed if an initial partial biopsy is inadequate for diagnosis or microstaging, but it should not generally be performed if the initial specimen meets criteria for sentinel lymph node biopsy
- **Punch biopsy** (different from punch excision): removes a small, cylindrical sample of the skin, including epidermis and dermis
- **Shave biopsy** (different from deep shave excision): removes a small upper layer of dermis; limit use to lesions with low suspicion of melanoma as there is a high risk for sampling error

Pathology Report

- The clinician must provide the following data to the pathologist: patient identification, type of biopsy, size of specimen, ABCDE criteria, dermoscopic features or photos (if available), age and sex of patient, and precise anatomic location (e.g., forearm, hand) of the biopsy site, including laterality, to reduce chances of subsequent wrong-site surgery.
- An essential element of the report is the status of the peripheral and deep margins (positive or negative) of the specimen.

Tumor Staging and Treatment (Buzaid & Gershenwald, 2023)

Staging and prognosis of cutaneous melanoma are based on the eighth edition American Joint Committee on Cancer (AJCC) tumor, node, metastasis (TNM) system. This system includes:

- Information about the primary tumor (T): presence, thickness (Breslow depth), ulceration status
- Regional lymphatics (N): metastasis to the proximal lymph nodes
- Distant metastatic sites (M), and for patients with stage IV disease only, serum lactate dehydrogenase (LDH).

For complete staging information, please refer to this poster, AJCC Melanoma of the Skin Staging. Other prognostic factors include age, sex, sentinel lymph node tumor burden, mitotic rate, and circulating tumor DNA (ctDNA) or melanoma cells.

Melanoma Stage and Treatment		
Stage	**Tumor Depth and Metastasis**	**Treatment**
Stage 0 (melanoma in situ)	Tumor is limited to the epidermis (melanoma in situ); no regional or distant metastases	Surgical removal with a margin of normal skin surrounding the melanoma
Stage I	Low-risk primary melanoma; localized tumor, 1-2 mm thick with or without ulceration and involves epidermis, dermis, or subcutaneous tissue; no spread to the lymph nodes or distant metastases	Surgical removal with a margin of normal skin; sentinel lymph node (SLN) biopsy may be performed prior to excision to check for metastasis; SLN biopsy is recommended for tumor thickness greater than 0.75 mm
Stage II	Primary tumors are at higher risk of recurrence; localized tumor may be greater than 2 mm thick and involve muscle	SLN biopsy and surgical excision with wide margin of normal skin; immunotherapy may be prescribed
Stage III	Invasion of the regional lymph nodes, but no metastasis to other parts of the body	Surgical removal with wide margin of normal skin and removal of regional lymph nodes to help prevent spread of disease; adjuvant therapy like immunotherapy, chemotherapy, and radiation may be utilized to prevent spread
Stage IV	Presence of metastases, spread to lymph nodes that are distant from the original tumor or spread to internal organs (e.g., lung, liver, brain, bone, and GI tract)	Difficult to treat; surgical excision of lesions or lymph nodes in addition to aggressive immunotherapy, chemotherapy, and radiation therapy

Imiquimod and Radiation Therapy (Swetter et al., 2019)

- Topical imiquimod 5% cream may be used as second-line treatment for melanoma in situ, lentigo maligna type when surgery is not possible; carefully discuss the risks and benefits with the patient and family.
- For nonsurgical candidates, radiation therapy may be utilized as a second-line therapy for melanoma in situ, lentigo maligna type; consultation with a radiation oncologist is recommended to review the risks and benefits of radiation therapy.
- Management of advanced cutaneous melanoma will include (Sosman, 2024):
    - Checkpoint immunotherapy inhibition with programmed cell death 1 (PD-1) inhibitor (pembrolizumab, nivolumab) in addition to ipilimumab.
    - Targeted therapy for specific gene mutations
    - Cytotoxic chemotherapy

Tumor Surveillance (Swetter et al., 2019)

- Schedule regular clinical follow-ups for full skin exams and assessment of lymph nodes.
- Collaboration with medical oncology is recommended for patients with high-risk cutaneous melanoma and those with a positive sentinel lymph node biopsy result.
- Educate patients and family members to perform regular skin self-exams and to look for:
    - New moles
    - Moles that look abnormal
    - Change in size, shape, color, or texture of mole or birthmark
    - Wound that doesn't heal
    - Recurrent disease or new primary cutaneous melanoma
    - Regional lymph node enlargement

Genetic Counseling (Swetter et al., 2019)

Cancer risk counseling by a qualified genetic counselor is recommended for patients who have:

- A family history of invasive cutaneous melanoma or pancreatic cancer (3 or more affected members on one side of the family)
- Multiple primary invasive cutaneous melanoma (3 or more), including one early-onset tumor (at age less than 45 years)
- One or more melanocytic BAP1-mutated atypical intradermal tumors and a family history of mesothelioma, meningioma, and/or uveal melanoma
- Two or more melanocytic BAP1-mutated atypical intradermal tumors

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