Skin Cancer

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KEYWORDS

• Basal cell carcinoma • Squamous cell carcinoma • Melanoma • Dermoscopy • Excision margin • Melanonychia • Histopathologic

KEY POINTS

- Cancer of the skin is the most common type of cancer in humans. Melanoma accounts for only 2% of all skin cancers but causes most skin cancer deaths.
- Melanoma is more than 20 times more common in white people than in African Americans. Individuals with fair skin and chronic sun exposure are at the highest risk for melanoma but other factors also contribute to the overall risk.
- Definitive diagnosis of skin malignancy is usually made with skin biopsy and histopathologic examination; history and physical examination are key components to diagnosing skin malignancies. Skin biopsy types include excisional biopsy, punch biopsy, and shave biopsy.
- Dermoscopy seems to increase sensitivity in detecting skin cancers and a working knowledge of this modality can be helpful in the primary care setting.
- Prevention measures include the appropriate use of sunscreen, minimizing sun exposure, wearing hats and long clothing while exposed to the sun, and avoiding tanning beds.

INTRODUCTION

Skin cancer is the most common form of cancer in the United States. Most skin cancers are nonmelanomatous. Malignant nonmelanoma skin cancers originate from keratinized epithelial cells. These cancers include basal cell carcinoma (BCC) and squamous cell carcinoma (SCC). Melanoma only accounts for about 2% of malignant skin cancer but causes most deaths. More than 2 million cases of skin cancer were diagnosed in the United States in 2010. BCC is the most common form and is usually slow growing and locally invasive. SCC is the second most common form of nonmelanomatous skin cancer, accounting for approximately 20% to 30% of cases.[1–3]

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The most important risk factor is chronic ultraviolet exposure. Diagnosis is usually suspected in older, fair-skinned individuals with scaly, indurated lesions on sun-exposed areas, primarily on the head and neck. Accuracy of clinical diagnosis can be enhanced using magnification, adequate lighting, and a dermatoscope. Biopsy with histopathologic confirmation is required for definitive diagnosis. Full-thickness biopsy is required for evaluation of melanoma because management and prognosis depend on the depth of the lesion. Overall cases of all forms of skin cancers have been increasing across the world.

Some studies have shown an increase in melanoma incidence among young individuals, with some epidemiologic studies showing as much as a 50% incidence in individuals aged 35 to 65 years. Working knowledge of these common malignancies is important in primary care settings. If there is a suspicion of a skin cancer lesion, a biopsy should be performed or a referral to a dermatologist should be initiated.

SKIN BIOPSY

Indication to Biopsy

- Suspected neoplastic lesions
- Bullous disorders
- If diagnosis is unclear and/or for therapeutic purposes

Contraindications to Biopsy

Contraindications to biopsy include infected site (if diagnosis of infection is not what is being considered), bleeding disorders, and patients on blood thinners.

Patients should not be taken off therapeutic or prophylactic blood thinners for a skin biopsy. These patients may benefit from being referred to a dermatologist if it is thought that hemostasis will be a problem. Lesions on the face, eyelids, and lips may need to be referred to a dermatologist or plastic surgeon because they are in readily visible locations.

Patients should be asked about allergies to topical antibiotics, antiseptics, local anesthetics, and tape, as well as bleeding disorders and any use of blood-thinning medications.

Site Selection

- Thickest, most pigmented area
- Area with most inflammatory changes
- For blistering lesions, a newly formed vesicle should be chosen
- Bullae should be biopsied at their edge

Types of Skin Biopsy

- Punch
- Shave
- Excision

Punch Biopsy

- Not a sterile procedure
- The site should be prepared with isopropyl alcohol, povidone-iodine, or chlorhexidine
- The site should be anesthetized with 1% to 2% lidocaine
- Epinephrine may be added to lidocaine if the site is not at the digits, ears, or nose
- A disposable round knife punch may be used
- May be used to excise small lesions

- Size ranges from 2 mm to 10 mm
- Biopsy is taken to the depth of the subcutaneous tissue
- Skin may heal by secondary intention
- Either 1 or 2 sutures may be used for better cosmetic results in larger punch biopsies
- Single-layer simple interrupted sutures are adequate
- Patients should be instructed to keep the area clean and to apply ointment such as bacitracin twice daily
- Biopsies not sutured should be covered with clean gauze and changed twice daily

Shave Biopsy

- Not a sterile procedure
- The site should be prepared with isopropyl alcohol, povidone-iodine, or chlorhexidine
- The site may be anesthetized with 1% to 2% lidocaine
- Wheal of anesthesia may be used to raise the lesion to aid the ease of the biopsy
- May add epinephrine to lidocaine if the site is not at the digits, ears, or nose
- Performed with 15-blade scalpel or double-edged razor
- Ideal for raised lesions and lesions confined to the epidermis
- This technique should not be used for a pigmented lesion or a lesion suspicious for melanoma
- Sutures are not necessary
- May leave a depressed scar once healed
- Patients should be instructed to keep area clean and apply ointments such as bacitracin twice daily
- The biopsy site should be covered with gauze and changed twice daily after cleaning

Excisional Biopsy

- Sterile procedure
- The site should be prepared with isopropyl alcohol, povidone-iodine, or chlorhexidine
- The site may be anesthetized site with 1% to 2% lidocaine
- Epinephrine may be added to lidocaine if the site is not at the digits, ears, or nose
- Performed with a scalpel
- Biopsy is taken to the depth of the subcutaneous tissue
- Ideal for lesions that are large, known to be malignant, or are typical of a malignancy
- Sutures are necessary
- Patients should be instructed to keep the area clean and apply ointments such as bacitracin twice daily

BASAL CELL CARCINOMA

BCC is a skin cancer that originates from the basal layer of the epidermis and its appendages. It is caused by cell mutations induced by ultraviolet radiation and thus arises most commonly on sun-exposed areas, such as the nose, ears, face, and backs of hands; however, it may occur anywhere on the body. It is a slow-growing cancer that rarely metastasizes.

Epidemiology

It is estimated by the American Cancer Society that approximately 3.5 million nonmelanoma skin cancers were treated in the United States in 2006. It is thought that 80% or greater of these skin cancers were BCC. This cancer is more common among white people and the incidence in men is 30% higher than in women. The lifetime risk of developing BCC is 30%. The incidence of BCC increases with age and proximity to the equator. Approximately 40% of individuals diagnosed with BCC develop another lesion within 5 years.[4–6]

Risk Factors

Risk factors for BCC are identical to those of other skin cancers (sun exposure, fair complexion, light eyes) but also include:

- Ionizing radiation
- Chronic arsenic exposure
- Basal cell nevus syndrome (Gorlin syndrome), which is an autosomal dominant mutation of the human patched gene

Clinical Presentation

BCC can be divided into 3 main subtypes: superficial, nodular, and morpheaform. The nodular variant makes up approximately 60% of cases, superficial BCC accounts for another 30%, and morpheaform BCC occurs 5% to 10%. Each group has its own distinct physical characteristics and histologic findings.[1,6–8]

Nodular Basal Cell Carcinoma

Nodular BCC most commonly presents on the face as a pearly, skin-colored, or pink papule. The papule typically has a translucent pearly appearance, telangiectasias, and may have ulceration (**Fig. 1**).

Superficial Basal Cell Carcinoma

Superficial BCC typically appears on the trunk, presenting as an erythematous, scaly papule or plaque. The border of the lesion may be lined with translucent papules and the center of the lesion may appear atrophic (**Fig. 2**).

Fig. 1. Nodular BCC.

Fig. 2. Superficial BCC. (*From* National Cancer Institute/Kelly Nelson. Basal cell carcinoma, superficial. Available at: https://visualsonline.cancer.gov/details.cfm?imageid=9236.)

Morpheaform Basal Cell Carcinoma

Morpheaform BCC presents as an erythematous or skin-colored papule or plaque. The lesion may appear scarlike with induration, atrophy, and irregular borders (**Fig. 3**).

Treatment

BCC is easily treated in the outpatient setting. Electrodessication and curettage or local excision is curative. Mohs micrographic surgery may be used in cosmetically

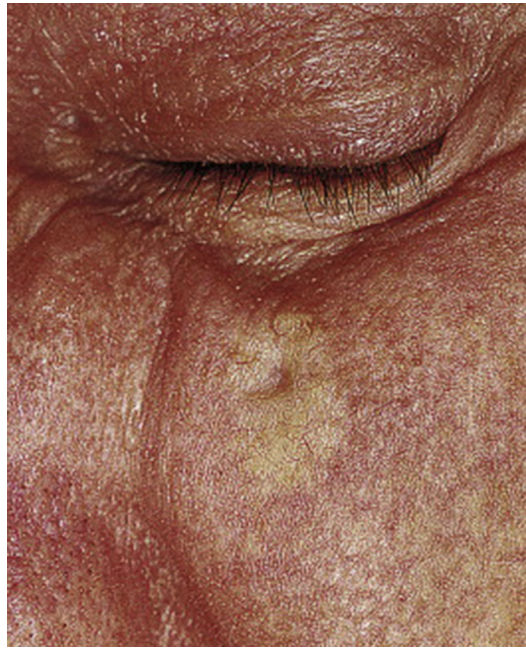

Fig. 3. Morpheaform BCC. (*From* Habif TP, Campbell JL, Chapman MS, et al. Premalignant and malignant non-melanoma skin tumors. In: Gabbery R, editor. Skin disease. 3rd edition. Philadelphia: Saunders; 2011. p. 470; with permission.)

sensitive areas such as eyelids, ears, nose, and lips, or for larger or recurrent lesions. Topical imiquimod 5% cream can also be used to treat superficial BCC.[9]

SQUAMOUS CELL CARCINOMA

Cutaneous SCC arises from malignant, uncontrolled proliferation of epidermal keratinocytes. Like BCC, SCC is also caused largely by ultraviolet radiation.

Epidemiology

Cutaneous SCC is the second most common skin cancer. The exact percentage of cutaneous SCC cases in the United States is not known because they are usually not reported to cancer registries. The incidence of SCC in the United States is estimated to be around 20% of nonmelanoma skin cancer cases.[1,7]

Bowen Disease

Bowen disease is the intraepithelial form of SCC, also known as SCC in situ. Bowen is associated with human papillomavirus in addition to typical skin cancer risk factors. It is confined to the epidermis and does not infiltrate the dermis. It presents as a rough, scaly, erythematous plaque with irregular borders. Most cases present on the lower legs and sun-exposed skin, and are found in women. However, this lesion can appear in any location. Because Bowen disease is confined to the epidermis, unlike invasive SCC, effective treatment can be seen with cryotherapy, cauterization, and topical 5-fluorouracil.

Erythroplasia of Queyrat

Erythroplasia of Queyrat is a form of SCC in situ that presents on the glans or prepuce of the penis in men and the vulvae in women. Like Bowen disease, the atypical malignant squamous cells are confined to the thickness of the epidermis. This condition is associated with the human papillomavirus. For this reason, erythroplasia of Queyrat is also called Bowen disease of the glans penis. The lesion presents as an erythematous scaly or crusting plaque that may have bleeding and/or ulceration. Cases are almost exclusively seen in middle-aged uncircumcised men. Effective treatment is readily achieved with the same modalities as in Bowen disease.

Risk Factors

Risk factors for SCC are identical to those of BCC but also include the following:

- Chronic inflammation caused by a laceration, scar, burn, ulcer, or other skin damage
- Epidermolysis bullosa syndromes (a group of skin diseases that make individuals prone to forming bullae on the skin without a traumatic event to the skin)

Clinical Presentation

Similar to other skin cancers, SCC most commonly presents on sun-exposed areas, but can develop anywhere on the body. SCC commonly presents as rough, erythematous papules, plaques, and nodules with well-demarcated borders and crusting. The lesions may show ulceration, pigmentation, erythema, scaling, or hyperkeratosis (**Fig. 4**).

Diagnosis

A diagnosis is made via biopsy of the lesion and histopathologic examination. Shave, punch, or excisional biopsies are all acceptable methods for suspected SCC diagnosis.

Fig. 4. SCC. (*From* Squamous cell carcinoma. National Cancer Institute. Available at: https://visualsonline.cancer.gov/details.cfm?imageid=2165.)

Treatment

Treatment of SCC is similar to that of BCC and can be handled in an outpatient setting. Because of the increased risk for metastasis, surgical excision or Mohs surgery is preferred to electrodessication and curettage. Surgical excision should be performed with a goal of a margin of 4 mm to 6 mm. Radiation therapy is an option for larger cancers or in patients who are not candidates for surgical intervention.

Risk Factors for Recurrence of Cutaneous Squamous Cell Carcinoma

- Location
- Size
- Poorly defined borders
- Recurrent tumors
- Immunosuppressed patient
- Site of previous radiation therapy or chronic inflammation
- Rapidly growing tumor
- Neurologic symptoms
- Moderately or poorly differentiated tumor
- Adenoid, adenosquamous, or desmoplastic subtypes
- Depth greater than or equal to 2 mm or Clark level IV–V[9]
- Perineural or vascular involvement

MELANOMA

Melanoma is an aggressive malignant neoplasm derived from melanocytes. Melanocytes are found in the basal layer of the epidermis. When they are exposed to ultraviolet light there is an accumulation of genetic mutations that activate oncogenes, inactivate tumor suppressor genes, and impair DNA repair. This process may lead to uncontrolled proliferation of melanocytes and ultimately melanoma.

For patients with cutaneous melanoma, the prognosis is related to the location and depth of the primary tumor, and the presence or absence of localized and distant metastatic disease.

There are 4 major subtypes of invasive cutaneous melanoma that are grouped for their distinct histologic patterns: superficial, nodular, lentigo maligna, and acral lentiginous.

Epidemiology

Estimates for 2014 are that 76,100 invasive melanomas will be diagnosed in the United States and that melanoma could claim 9710 lives. Melanoma is the fifth most common cancer in men and the seventh in women in the United States.

The incidence rates for invasive melanoma among white individuals in the United States in the years 2006 to 2010 were 27.4 per 100,000 men and 16.7 per 100,000 women per year (Fig. 5). From 1992 to 2006, the incidence increased by more than 3% per year among non-Hispanic white people. The increase was observed in both sexes and in all age groups and was highest in individuals aged 65 years and older.[7]

Superficial Melanoma

Superficial melanoma is the most common subtype and makes up 75% of malignant melanomas. Histologic findings in this subgroup are a radial growth before growing vertically into deeper tissue layers. During this radial growth phase the melanoma spreads by single-cell dispersal. Once nests of neoplastic melanocytes reach past the papillary dermis and the dermal layer the lesion is considered to be in its vertical growth phase. Superficial melanoma occurs more frequently on the backs in men and the lower extremities in women. The lesion may present with variable colors (black, blue, brown, white, gray, red), irregular borders, and an asymmetric flare at the lesion's border that represents the advancing proliferation of melanocytes (Fig. 6).[4,10,11]

Nodular Melanoma

Nodular melanoma is an aggressive, vertically growing melanoma that comprises 15% to 30% of melanomas. It does not have a radial growth phase, thus growing in depth more quickly than in width. For this reason, it may take longer for a person to be suspicious of the lesion. Nodular melanoma commonly present as darkly pigmented pedunculated or polypoid nodules (Fig. 7).

Lentigo Maligna Melanoma

Lentigo maligna melanoma is the second most common subtype of melanoma. It most commonly presents on sun-exposed areas as a small, flat, tan, irregular-bordered, asymmetric macule that, over time, enlarges and begins to vary in color (Fig. 8).

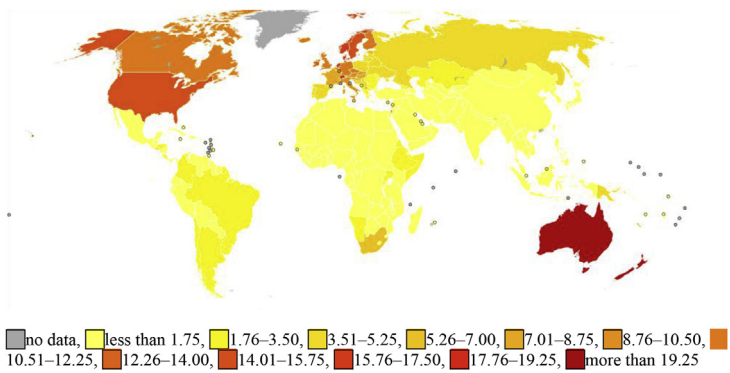

Fig. 5. Age-standardized incidence rate of melanoma of the skin per 100,000 inhabitants in 2008.

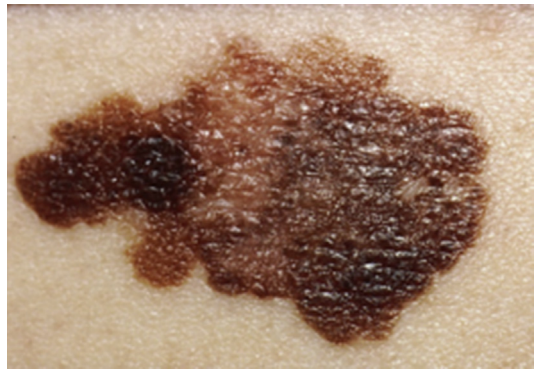

Fig. 6. Superficial melanoma. (*From* National Cancer Institute (AV number: AV-8500-3850; date created: 1985; date entered: 1/1/2001). Available at: http://visualsonline.cancer.gov/details.cfm?imageid=2184.)

Acral Lentiginous

Acral lentiginous melanoma most commonly appears in palmar, plantar, and subungual locations (**Fig. 9**). This melanoma is the least common subtype and accounts for fewer than 5% of cases. However, compared with white people, the rates in Asians, Chinese, Japanese, African, and Middle Eastern people is significantly higher.[12,13]

Subungual melanoma most commonly presents as longitudinal melanonychia, which is a black or brown pigmentation of the normal nail plate (**Fig. 10**). The added involvement of the proximal nail fold, known as Hutchinson sign, is also an indicator of a malignant cause. Transverse melanonychia without Hutchinson sign suggests a benign cause. Melanonychia may be a normal finding in dark-skinned individuals as a result of trauma, or a postinflammatory event.

Melanonychia Differential

- Chronic paronychia
- Onychomycosis
- Subungual hematoma
- Pyogenic granuloma
- Glomus tumor
- Subungual verruca
- Mucous cyst

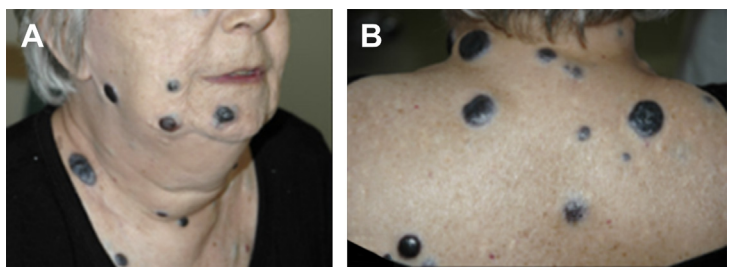

Fig. 7. Nodular melanoma. (*From* Rathi VK, Williams RB, Yamrozik J, et al. Cardiovascular magnetic resonance of the charcoal heart. J Cardiovasc Magn Reson 2008;10:37.)

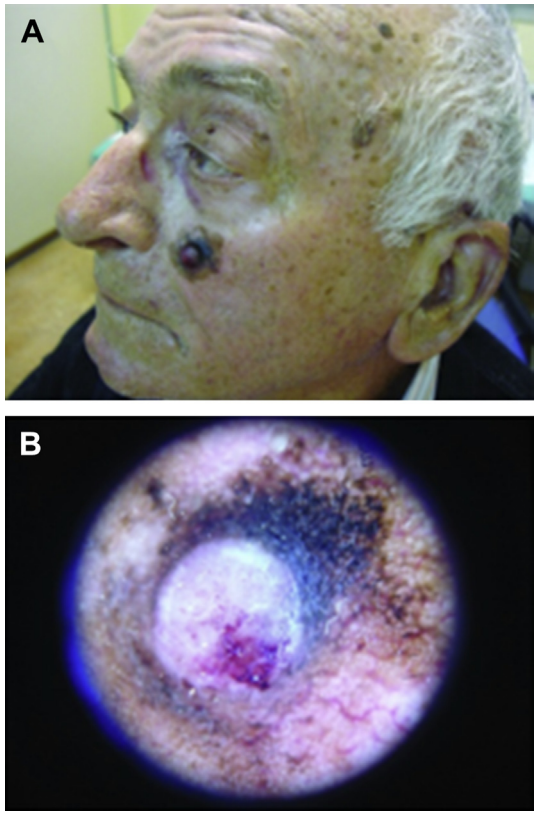

Fig. 8. (*A*) Histologically confirmed lentigo maligna melanoma on left cheek of an elderly male patient, arising from a lentigo maligna after many years. (*B*) Dermoscopic view of lentigo maligna melanoma. (*From* Tsatsou F, Trakatelli M, Patsatsi A, et al. Extrinsic aging: UV-mediated skin carcinogenesis. Dermatoendocrinol 2012;4(3):295.)

- Subungual fibroma
- Keratoacanthoma

Risk Factors

Risk factors for melanoma include:

- The presence of a high number of common nevi
- One or more atypical nevi
- Light skin
- Excessive sun exposure
- History of sunburns
- Tanning bed exposure
- Older age
- Family history in first-degree relatives

Clinical Presentation

Nevi that have the following characteristics (Fig. 11):

Fig. 9. Acral lentiginous melanoma on the plantar surface. (*From* Bristow IR, Acland K. Acral lentiginous melanoma of the foot and ankle: a case series and review of the literature. J Foot Ankle Res 2008;1(1):11.)

- Asymmetry
- Irregular borders
- Variegated color
- Diameter greater than 6 mm
- Recent change including size color and shape
- Inflammation

Fig. 10. (*A*) Black to brown pigmented patch on the left ring finger. (*B*) Patient 7: irregularly pigmented patch on the right heel. (*From* Park HS, Cho KH. Acral lentiginous melanoma in situ: a diagnostic and management challenge. Cancers (Basel). 2010;2(2):643.)

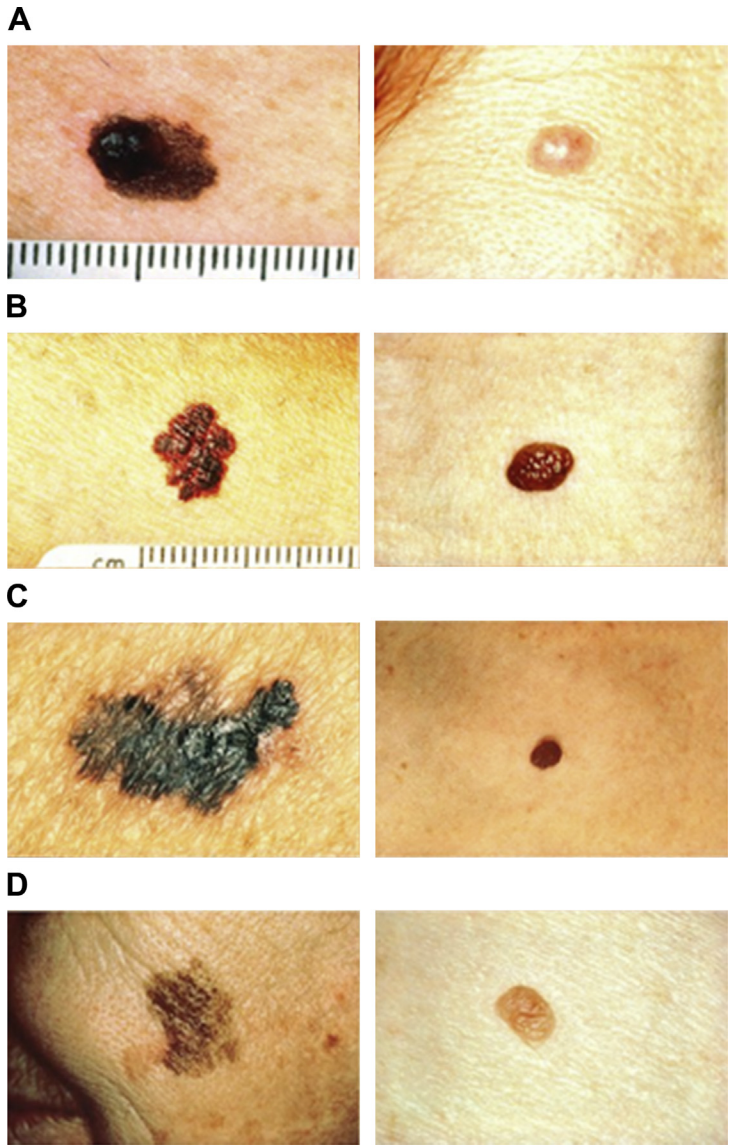

Fig. 11. ABCD rule. Melanomas showing (*A*) asymmetry; (*B*) a border that is uneven, ragged, or notched; (*C*) coloring of different shades of brown, black, or tan; and (*D*) diameter that had changed in size. The normal moles on the right side do not have abnormal characteristics (no asymmetry, even border, even color, no change in diameter).

- Bleeding or crusting
- Sensory change

When evaluating patients with multiple nevi it may be helpful to use the so-called ugly-duckling sign. This sign is based on the observation that nevi, although numerous, all tend to have a similar morphology. However, a lesion with a different morphology from surrounding lesions should be considered suspicious.

Using a dermatoscope to further evaluate the characteristics of a lesion in the clinical setting may be of some use (Fig. 12). However, the help it may provide in detecting melanoma is limited by the operator's training in dermoscopy. A meta-analysis of dermoscopy examinations compared with naked-eye examination in the diagnosis of melanoma concluded that, for clinicians with at least some training in dermoscopy, the addition of dermoscopy to the unaided clinical examination increases the sensitivity in detecting melanoma (90% vs 71%), but has similar specificity (80% vs 90%).

Diagnosis

Histopathology is the gold standard of diagnosis. A biopsy should be performed of any lesion that is suspected to be melanoma. If it is unclear whether a lesion is benign or if indication for biopsy is unclear the patient should be referred to a dermatologist. An excisional biopsy that includes the entire lesion with 1-mm to 3-mm margins of normal skin and part of the subcutaneous fat should be performed whenever possible. A shave biopsy should not be used if melanoma is suspected because the depth of the lesion is vital for staging purposes. An excisional biopsy has the added benefit of being diagnostic as well as therapeutic.

Treatment

Once a diagnosis has been made by biopsy of the lesion, pathologic staging must be completed to determine prognosis and treatment. Staging is as follows:

- Stage 0 (in situ): melanoma confined to the epidermis; recommended excision margin, 0.5 to 1 cm
- Stage I: less than or equal to 1 mm thick; 10-year survival, 92%; recommended excision margin, 1 cm
- Stage II: 1.01 to 4.00 mm thick; 10-year survival, 80%; recommended excision margin, 2 cm
- Stage III: melanoma has spread to nearby lymph node; 10-year survival, 63%
- Stage IV: melanoma has spread to an internal organ, lymph node far from the original melanoma, or is found on the skin far from the original melanoma; 10-year survival, 50%[14]

Fig. 12. Dermatoscope.

A sentinel lymph node biopsy should be considered for patients with primary melanoma larger than 1 mm or a primary melanoma smaller than 1 mm with negative prognostic features.

Monitoring

At present there are no randomized trials to evaluate screening effectiveness. A 2009 update from the United States Preventive Services Task Force found insufficient evidence to recommend for or against either routine screening of the general population for skin cancer by primary care providers or counseling patients to perform periodic skin self-examinations.

The American Academy of Dermatology recommends that those at highest risk, having a strong family history of melanoma and multiple atypical moles, should perform frequent self-examination and seek professional evaluation of the skin at least once per year.

Skin Cancer Prevention

Prevention is focused on proper protection from the sun whenever possible. Proper protection includes:

- Sun avoidance
- Full-length clothing that covers exposed skin
- Hats and sunglasses
- Use of broad-spectrum (ultraviolet A/ultraviolet B) sunscreen and sunblock with frequent reapplications
- Avoiding tanning bed exposure

It is vital that discussion of skin cancer prevention is incorporated into the counseling of patients at all well-child and adult wellness visits.

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