Melanoma
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What is Melanoma?
• Most dangerous form of skin cancer
• Begins in melanocytes, which are the pigment-producing cells of the skin

Lifetime Risk
• Risk of being diagnosed with melanoma:
  – Males: 2.54% (1 in 39)
  – Females: 1.60% (1 in 63)
  – Elderly men are at the highest risk
  – Most common cancer diagnosis for age 25-29
  – 2nd most common cancer diagnosis for age 15-29
• Risk of dying from melanoma:
  – Males: 0.43% (1 in 233)
  – Females: 0.21% (1 in 476)

Risk Factors
• Sun exposure, sun exposure, sun exposure
• Tanning Beds
• Severe, blistering sun burn
• Fair skin
• Dysplastic nevi
• More than 50 moles
• Weakened immune system

Rate of increase of diagnosed cases of melanoma compared to other cancers

What to look for? “ABCD”
• Asymmetry
• Border that is irregular
• Color that is uneven
• Diameter
Also note:
• Itching
• Increase in size or number
• Ulceration or bleeding
Appearance of melanoma

- Brown or black in color (melanin producing)
- Pink, tan or white (non-melanin producing)

Usually occurs on back, legs, neck and face, less common in eyes, genitals, mouth and anal areas

Diagnosis: types of biopsies

- Shave Biopsy
- Punch Biopsy
- Excisional Biopsy

Pathology: all about DEPTH

- Breslow’s thickness: the total vertical height of the melanoma; in millimeters
- Clark’s level: describes the level of anatomical invasion of the melanoma in the skin

3 cancer idioms

- The more the better
- Less is more
- The longer you wait, the worse it will get

<table>
<thead>
<tr>
<th>Stg</th>
<th>T-N-M</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>TIS, N0, M0</td>
<td>Confined to epidermis (top layer skin)</td>
</tr>
<tr>
<td>1</td>
<td>T1a-2a, N0, M0</td>
<td>Confined to skin, now thicker (&lt; 1.0ml)</td>
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<td></td>
<td></td>
<td>• 1b = ulcerated</td>
</tr>
<tr>
<td>2</td>
<td>T2b, -4b, N0, M0</td>
<td>Thickness increased (1.01 to &gt; 4.0ml)</td>
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<td></td>
<td>• 2b = ulcerated</td>
</tr>
<tr>
<td>3</td>
<td>T1a-4b, N1a-3, M0</td>
<td>Spread to &gt; 1 nearby lymph node (LN) or skin</td>
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<tr>
<td>4</td>
<td>Any T, any N, M1</td>
<td>Spread to an internal organ, distant LN or distant skin site</td>
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Histologic Classification

Frequent description:

Malignant Melanoma
- with or without ulceration

Cutaneous Melanoma

Most Common
- Superficial spreading
- Nodular
- Lentigo maligna
- Acral lentiginous

Less Common
- Mucosal Lentiginous
- Desmoplastic
- Ocular
- Verrucous

Prognosis

- Cutaneous melanomas arising in the head and neck area, trunk, and possibly the lower extremity have a worse prognosis than those arising on the upper extremity
- Site of the primary tumor is less important than the factors including tumor thickness, mitotic rate, ulceration and nodal involvement.
- Acral melanomas (subungual, palmar/plantar) are also associated with a poorer prognosis than other cutaneous melanomas

Earlier stage, generally better survival

New cases and 5 year survival

Initial Management

- Surgery
- Sentinel lymph node biopsy
- Lymph node dissection
- Radiation

Stage I or II

- Surveillance
  - Need to establish care with a dermatologist
  - Frequent full body skin exams
    - Every 3-6 months for the first two years, then every 6-12 months
    - Assess lymph nodes at each visit
  - Blood tests and radiologic imaging is not recommended
  - Ensure early detection of recurrence
    - Local, in-transit, nodal, or distant

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Stage III

Adjuvant therapy for stage III

- Treatment given after surgery to prevent recurrence in order to stop/slow growth of remaining microscopic disease not removed during surgery
- Stage III at high risk for recurrence, both locally and distant
- Immune therapy, biochemotherapy and vaccines
- Acute observation

Adjuvant Therapy

Stage IIIa & IIIb
- Immunotherapy
  - High-dose interferon
  - PEGylated interferon
- Shown to increase relapse free survival
- Debate on whether interferon improves overall survival
- Flu-like side effects

Stage IIIc
- Dependent on tumor size, tumor burden, and anatomic location
- Surgical excision
- Local therapies: laser ablation, external beam radiation, intralesion injections, topical creams
- Regional therapies: hyperthermic isolated limb perfusion (HILP) and isolated limb infusion (ILI)
- Clinical Trials

Statistics

Advanced or Metastatic Melanoma

- Management options include:
  - Surgical Resection
  - Immunotherapy: stimulate your own immune system to stop or slow the melanoma cells
  - Targeted Therapy: inhibit specific enzymes or molecules important to cancer cell growth
  - Chemotherapy: stop or slow the growth by interfering with the cell’s ability to divide or reproduce
  - Radiation therapy
  - Clinical Trial
  - Palliative Treatment
Metastatic Melanoma: Surgery

• May be recommended if melanoma has spread to one or a very limited number of sites.
• May prolong survival or relieve symptoms
• Surgery is rarely curative
   — Likely microscopic disease elsewhere in the body

Metastatic Melanoma: Chemotherapy

• Melanoma has always been considered “chemo-resistant”
• Dacarbazine is the only FDA approved chemotherapy drug for the treatment of metastatic melanoma.
• Carboplatin, paclitaxel (Taxol) and bevacizumab (Avastin) has shown some success
• Limited duration of response- usually 6-8 months
• Biochemotherapy: Combination of biologic therapy (interferon, IL-2) and chemotherapy (cisplatin, dacarbazine, vinblastine)

Metastatic Melanoma: Radiation Therapy

• Rarely used to treat primary melanoma
• Main role is relief symptoms when metastasized to areas such as the brain or bone
   — Cannot cure advanced disease, but can shrink tumors that cause discomfort
• Occasionally used for stage III melanoma to prevent recurrence in lymph node region

Immunotherapy

“Immunotherapy: Using the Body to Fight Cancer”

• Interleukin-2
  — Cytokine which helps activate the immune system (including T cell and natural killer cells) to kill cancer cells
  — FDA approved in 1998
  — The use of IL-2 has declined due to newer therapies
  — Significant toxicities associated with treatment including vascular leakage, kidney and respiratory failure
  — Requires inpatient ICU stay
  — IL-2 shrinks tumors in about 15% of patients. However, about 5% of patients get a complete response that can last 7 years or more.
Immunotherapy

- Ipilimumab (Yervoy)
  - FDA approved in March 2011
  - Monoclonal antibody designed to block the CTLA-4 receptor
  - CTLA-4 deactivates the T cell = decreased immune response
  - Blocking CTLA-4 unleashes the immune response
  - Immune response is not specific to only melanoma
    - Can cause auto-immune toxicities

- PD-1 Inhibitor (Keytruda and Nivolumab)
  - FDA approved in 2014
  - Monoclonal antibody
  - Blocks the interaction between PD-1 and its ligand, PD-L1
    - inhibition of the interaction between PD-1 and PD-L1 can enhance T-cell responses
  - Unresectable stage III or stage IV
  - May be given alone or in combination with ipilimumab

Targeted Therapies

- Destroy cancer cells while leaving normal cells intact
- BRAF inhibitors include vemurafenib (Zelboraf) and dabrafenib (Tafinlar)
  - Dabrafenib may be given in combination with a MEK inhibitor (trametinib)
- Alone vs. combination
- Continuous vs. intermittent

Metastatic Melanoma: Targeted Therapies

- Designed to interfere with the specific molecules that are driving the growth and spread of the tumor

Imlygic

a modified herpes simplex virus 1
- (normally causes cold sores)
Genetically modified
- Attenuates the virus (so it can no longer cause herpes)
- Increases selectivity for cancer cells (so it destroys cancer cells while leaving healthy cells unharmed)
- Secretes the cytokine GM-CSF (a protein naturally secreted in the body to initiate an immune response)
pop quiz

Clinical Trials

- Often viewed as the best treatment option for late stage melanoma
- Monitored very closely
- Always have the option to discontinue participation
- Melanoma treatment is evolving very rapidly
- A clinical trial is the only way to receive a new therapy that may be better than the standard

Prevention

- Avoid the sun during the middle of the day
- Wear sunscreen year around
- Wear sun-protective clothing
- Stay away from tanning beds
- Become familiar with your skin and report any changes

Conclusion

- Early detection is key
- Treated with surgery alone when caught early
- Melanoma treatment is evolving rapidly
- Every patient should be screened for a clinical trial

Pale is the new tan
QUESTIONS???