METASTATIC CARCINOMA TO THE SKIN

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CONFLICTS

• No conflicts with the content of this lecture
METASTATIC CARCINOMA

- Relatively uncommon in comparison to primary cutaneous carcinomas.
- Requires high clinical suspicion.
- Gender differences.
- Clinical differential diagnosis.
- Histologic differential diagnosis.
METASTATIC CARCINOMA

- Skin metastasis is defined as the spread of malignant cells from a primary malignancy to the skin.
- Originate either from an internal malignancy or from a primary skin cancer (melanoma).
- Skin metastases are encountered in 0.7-9% of all patients with cancer.
- Skin is an uncommon site of metastatic disease when compared to other organs.
METASTATIC CARCINOMA

• Long-time lag between the diagnosis of the primary malignancy and the recognition of the skin metastases.

• Cutaneous metastasis may be the first indication of a clinically silent visceral malignancy.

• Regional distribution of the skin metastasis is related to the location of the primary malignancy and the mechanism of metastatic spread.

• The relative frequency of skin metastasis does not always correlate with the prevalence of the type of primary cancer (ie prostate cancer).
METASTATIC CARCINOMA

- Cutaneous metastasis as the first indication of an internal malignancy.
  - Lung.
  - Ovary
  - Renal
METASTATIC CARCINOMA
Mechanism of Metastatic Spread

- **Lymphatic Dissemination:**
  - Local overlying skin (Breast, Oral Cavity).

- **Hematogenous Dissemination:**
  - Local and/or Distant (Breast, Lung, GI, GU)
METASTATIC CARCINOMA

- Lung carcinoma (24%) is the most common skin metastasis in men (followed by large intestine 19%, melanoma 13%, oral cavity 12%).

- Breast carcinoma (69%) is the most common skin metastasis in women (followed by large intestine 9%).

- The anterior chest and neck region are the areas of greatest predilection in men.

- The anterior chest wall and the abdomen are the most commonly involved sites in women.
<table>
<thead>
<tr>
<th>Men</th>
<th>Women</th>
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<td><strong>&lt; 40 yr</strong></td>
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METASTATIC CARCINOMA

- Histologically, skin metastases usually show features reminiscent of the primary malignancy.

- Poorly differentiated - Carcinoma of Unknown Primary (CUP) - remember melanoma.

- Metastasis to the skin is often a pre-terminal event that heralds poor outcome.
METASTATIC CARCINOMA

- Benign vs. Malignant
- Primary skin cancer vs. Adnexal
- Primary skin cancer vs. Metastatic
- Adnexal carcinoma vs. Metastatic
- Epidermal involvement, depth/thickness dermis, resemble BCC/SCC, glandular differentiation
METASTATIC CARCINOMA
Benign vs. Malignant

- Size, Symmetry, Circumscription, Depth/Thickness
- Atypia, Mitoses, Differentiation
• Adnexal tumors (Benign and Malignant) usually lack epidermal continuity, involve the deep dermis, look different from a BCC/SCC, frequently display glandular differentiation

• Special stains - identify differentiation
METASTATIC CARCINOMA
Primary Skin Cancer vs. Metastatic

• Metastatic carcinomas usually lack epidermal continuity, involve deep dermis, look different from a BCC/SCC (exception metastatic SCC), frequently display glandular differentiation

• Special stains - identify differentiation
METASTATIC CARCINOMA
Adnexal Tumor vs. Metastatic

- Adnexal tumors (benign and malignant) and metastatic tumors usually lack epidermal continuity, involve deep dermis, look different from a BCC/SCC, frequently display glandular differentiation

- Benign adnexal tumors lack significant cytological atypia and show textbook architectural features

- Malignant adnexal tumors show cytological atypia and can have familiar architectural features and/or a remnant benign component

- Special stains - identify differentiation - P63 is key

- Remember melanoma markers!
Use of p63 expression in distinguishing primary and metastatic cutaneous adnexal neoplasms from metastatic adenocarcinoma to skin.

Ivan D, Nash JW, Prieto VG, Calonje E, Lyle S, Diwan AH, Lazar AJ.
Department of Pathology, University of Texas - M.D. Anderson Cancer Center
METASTATIC CARCINOMA
Clinical Presentation

- Skin metastases usually appear as non-specific groups of discrete firm painless nodules that emerge rapidly without any explanation.

- They vary in size from so tiny as to be of miliary lesions to as large as goose egg size.

- Some skin metastasis may mimic specific dermatological conditions such as cutaneous cyst, lipoma, dermatofibroma, pyogenic granuloma, hemangiomma, papular eruptions, herpes zoster eruptions, morpheaform plaques, alopecia, cellulitis and erysipelas.
METASTATIC CARCINOMA
Carcinoma of the Breast

- Inflammatory Metastatic Breast Carcinoma.
- En Cuirasse Metastatic Breast Carcinoma.
- Telangiectatic Metastatic Breast Carcinoma.
- Nodular Metastatic Breast Carcinoma.
- Alopecia Neoplastica.
- Metastatic Breast Carcinoma of the Eyelid.
METASTATIC CARCINOMA
Carcinoma of the Breast

• **Lymphatic dissemination:**
  
  • Inflammatory, En Cuirasse, Telangiectatic, Nodular including Inframammary Crease.

• **Hematogenous dissemination:**
  
  • Alopecia Neoplastica and Metastatic Breast Carcinoma of the Eyelid.
METASTATIC CARCINOMA
Inflammatory Metastatic Breast Carcinoma

- Erythematous patch or plaque with spreading border involving the breast and adjacent skin.
- Peau d’orange
- Erysipelas-like - aka Carcinoma Erysipeloides
METASTATIC CARCINOMA
Inflammatory Metastatic Breast Carcinoma

- Clusters of tumor cells involving superficial and deep lymphatics (retrograde lymphatic spread into the skin secondary to blockage of deep lymphatics)

- Capillary congestion (clinical erythema/warmth).

- Minimal inflammation.
METASTATIC CARCINOMA
En Cuirasse Metastatic Breast Carcinoma

- Cuirass = Armor vest
- Diffuse induration involving skin of the breast.
- Morphea-like.
METASTATIC CARCINOMA
En Cuirasse Metastatic Breast Carcinoma

• AKA Scirrhous Carcinoma

• Extensive fibrosis/sclerosis resulting in a rectangular punch biopsy.

• Inconspicuous fibroblast-like tumor cells - both solitary and single rows “Indian filing” between thickened collagen bundles.
METASTATIC CARCINOMA
Telangiectatic Metastatic Breast Carcinoma

- Violaceous papulovesicles on skin of the breast.
- Sometimes Lymphangiomata circumsptum-like.
METASTATIC CARCINOMA
Telangiectatic Metastatic Breast Carcinoma

- Tumor cells involving superficial lymphatics.
- Many prominent congested blood vessels immediately below the epidermis results in the clinical appearance of violaceous “vesicles”.
METASTATIC CARCINOMA
Nodular Metastatic Breast Carcinoma

- Multiple firm nodules with or without ulceration
- Inframammary crease frequently in women with large breasts.
- Solitary nodule can mimic primary cutaneous skin cancer.
METASTATIC CARCINOMA
Nodular Metastatic Breast Carcinoma

- Variably sized groups of tumor cells throughout dermis without epidermal connection.
- Glandular differentiation.
- Occasionally pigmented.
METASTATIC CARCINOMA
Alopecia Neoplastica

- Oval plaques or patches of scalp with hair loss.
- Cicatricial Alopecia vs. Alopecia Areata.
- Hematogenous.
METASTATIC CARCINOMA
Alopecia Neoplastica

• Resembles En Cuirasse (Scirrhous) Carcinoma.

• Extensive fibrosis/sclerosis with rectangular silhouette and reduction of hair follicles.

• Single rows of “Indian filing” tumor cells between thickened collagen bundles.
METASTATIC CARCINOMA
Metastatic Breast Carcinoma of the Eyelid

• Painless swelling with induration or a discrete solitary nodule.

• Chalazion vs. sebaceous carcinoma.

• Hematogenous.
METASTATIC CARCINOMA
Metastatic Breast Carcinoma of the Eyelid

• Nodular with glandular differentiation, lacks epidermal connection.

• Prominent histiocytoid appearance can result in misdiagnosis.

• Cytological atypia is present.
METASTATIC CARCINOMA
Immunohistochemical Stains

- Pan Cytokeratin +, CK7 +, CK20 usually negative.

- GCDFP-15 +, EMA +, CEA +

- ER/PR (positive or negative)

- Her2-Neu (positive or negative) - test mets for Her2 “gain”

- GATA3 - very helpful in triple negative breast cancer

- S100, HMB-45
GATA3 expression in breast carcinoma: utility in triple-negative, sarcomatoid, and metastatic carcinomas.
Treatment of HER2-Positive Metastatic Breast Cancer Following Initial Progression

Ingrid A. Mayer

Department of Medicine and Breast Cancer Research Program, Vanderbilt University School of Medicine
METASTATIC CARCINOMA
Carcinoma of the Breast

• Unusual histologic patterns:

• Signet ring cell pattern mimics primary signet ring cell carcinoma (eyelid, CK7+/CK20 +)

• Mucinous carcinoma pattern mimics primary mucinous carcinoma (eyelid, CK7+/CK20-).
METASTATIC CARCINOMA
Carcinoma of the Lung

• Most common metastatic carcinoma of the skin in men.

• Most common cause of cancer death in women.

• Localized cluster of papules or nodules on chest wall and back - occasionally solitary.

• Oat (small) cell - skin of the back.
METASTATIC CARCINOMA
Carcinoma of the Lung

- Small cell carcinoma - neuroendocrine.
- Non-small cell carcinoma (Squamous cell carcinoma and Adenocarcinoma)
METASTATIC CARCINOMA
Carcinoma of the Lung

- Small cell carcinoma vs Merkel cell carcinoma.
- Clinical history
- Multiple lesions
- Epidermal involvement
- Immunostains: CEA, CK20, TTF-1
METASTATIC CARCINOMA
Gastrointestinal Carcinoma

- Colorectal carcinoma is the 2nd most common type of primary carcinoma in men.

- Cutaneous metastases usually occur after the primary tumor has been recognized

- Abdomen and perineal area > Head and neck
• Gastric carcinoma is uncommon.

• Cutaneous metastases usually occur after the primary tumor has been recognized

• Any site - Umbilical most common
METASTATIC CARCINOMA
Gastrointestinal Carcinoma

• Histopathology shows glandular differentiation.

• Adenocarcinoma (abortive gland formation)

• Mucinous carcinoma pattern (pools of mucin, Large intestine)

• Signet ring cell pattern (single mucin-laden cells, Stomach)
METASTATIC CARCINOMA
Gastrointestinal Carcinoma

- Special stains
- Mucicarmine, Alcian Blue, Toluidine Blue
- CK20 positive CK7 negative
METASTATIC CARCINOMA
Sister Mary Joseph’s Nodule

- Gastrointestinal - 52%, colon, gastric, pancreatic
- Genitourinary - 28%, ovarian, uterine
- CUP - Carcinoma of Unknown Primary
- Hernia, endometriosis, keloid, omphalith
- Painful, Poor prognosis, Peritoneal metastases
METASTATIC CARCINOMA
Oral Cavity Carcinoma

- Primary - side of tongue or floor of mouth
- Lymphatic spread - face or neck.
- Multiple or solitary nodule(s) +/- Ulceration
- Virtually always Squamous cell carcinoma.
- Deep dermis/subcutis sparing upper dermis except ulcerated lesions - difficult to distinguish from primary cutaneous SCC.
METASTATIC CARCINOMA
Renal Cell Carcinoma

- Head and neck most common.
- Solitary or few nodules - tan-red to violaceous
- First sign or late lesion
- Virtually always in men
METASTATIC CARCINOMA
Renal Cell Carcinoma

- Clear cell adenocarcinoma
- Vascular
- Glycogen
- CD10 positive
METASTATIC CARCINOMA
Ovarian Carcinoma

- Abdomen (umbilicus), vulva, back
- Surgical scars
- Papillary Adenocarcinoma - Psammoma bodies
- Mucinous carcinoma
- CK7/CK20-positive
METASTATIC CARCINOMA
Miscellaneous Carcinoma

- Neuroendocrine carcinoma and carcinoid
- Liver
- Thyroid
- Adrenal
- Pancreatic
- Prostate
METASTATIC CARCINOMA
Prostate Carcinoma

- Skin Metastases - very uncommon
- Inguinal, thighs, lower abdomen
- Other sites (scalp) rare
- PSA, NKX3.1
A novel case of NKX3.1-positive metastatic cutaneous prostate cancer.

Wong JK, Minni JP, Nowak MA
What would I see on a report?

- Carcinoma involving dermis compatible with metastatic carcinoma
- Vascular/lymphatic involvement
- Special stains - P63, etc
- Prognostic studies ER/PR, Her-2-Neu
What do I do next?

- Very difficult phone call to patient
- Referral to oncologist or back to existing oncologist
- Possible additional biopsy for prognostic markers
- Palliative treatment including simple excision, PDT (Levulan), intralesional chemotherapy, local wound care, etc.
Summary

- Lymphatic vs. Hematogenous
- Gender differences
- Her2 for Breast Cancer
- Merkel - Small cell lung cancer
- Sister Mary Joseph - GI, ovary, pancreatic, renal
- Renal - glycogen in men “Sugarman”
- Prostate - NKX3.1, PSA