Clinical Vignettes in Dermatology

ASFA AKHTAR D.O., FAOCD, FAAD
DEPARTMENT OF DERMATOLOGY
CLEVELAND CLINIC FLORIDA
Basal Cell Carcinoma
Basal Cell Carcinoma (BCC)

- BCC is the most common skin cancer in humans
- Arises from the basal layer cells of the epidermis
- 30% of all malignancies
- Accounts for 70-80% of all cutaneous malignancies
Basal Cell Carcinoma (BCC)

- In 2006, the incidence was 2.6 million
- Continues to rise at an average rate of 4% to 8%
- Incidence of BCC is rising in the younger population
- Poses a significant health problem in terms of incidence and health care costs
Basal Cell Carcinoma (BCC)

- Ultraviolet radiation (UVR) is the most common factor in the pathogenesis of BCC
- The risk of developing BCC is higher in individuals who are fair and burn or tan easily versus individuals that those who are darkly pigmented
- Blistering sunburns in childhood increase the risk
- UV induced epidermal DNA damage is the primary carcinogenic insult leading to BCC formation
  - Eg. Xeroderma Pigmentosum
Basal Cell Carcinoma (BCC)

- Xeroderma pigmentosum (XP)
  - Hallmarks are photosensitivity, photophobia, and conjunctivitis
  - Patients lack the ability to repair UV induced DNA damage (defective DNA thymidine excision repair)
  - Multiple basal cell carcinomas, squamous cell carcinomas and melanoma develop in childhood
Basal Cell Carcinoma (BCC)

- The patched gene 1 (PTCH1) is a tumor suppressor gene mutated in patients with Basal cell nevus syndrome (Gorlin syndrome)
- Multiple BCCs, odontogenic cysts of the jaw, frontal bossing, pitting on the hands and feet, and ocular hypertelorism
- The usual age of development of BCC is 17-35 years
- The central face is mostly affected (eyelids, forehead, nose, upper lip and cheeks)
Basal Cell Carcinoma (BCC)

Other risk factors for the development of BCC include:

- Ionizing radiation
  - Acne
  - Tinea capitis
- Arsenic exposure
- Well water
- Fowler’s solution
- Industrial exposure (mining, smelting)
- Pesticides
- Topical Nitrogen mustard
- Scars
- Burns
Basal Cell Carcinoma (BCC)

Other syndromes associated with the development of BCC include:

- Basex syndrome
- Rasmussen syndrome
- Rombo syndrome
Basal Cell Carcinoma (BCC)

- Most basal cell carcinomas occur in sun-exposed areas
- 20% occur in sun-protected areas
- Men have a higher incidence than women
- Metastasis of BCC is very rare and ranges from 0.0028% to 0.1%
Basal Cell Carcinoma (BCC)

- Types of Basal Cell Carcinoma
  - Superficial
  - Nodular
  - Morpheaform
  - Infiltrative
  - Fibroepithelial
  - Infundibulocystic
Basal Cell Carcinoma (BCC)

- **Superficial BCC**
  - AKA superficial multicentric BCC
  - Dry, scaly lesion
  - Comprises at least 50% of BCCs
  - Favors the trunk and distal extremities but can occur on the head and neck
Basal Cell Carcinoma (BCC)

- **Superficial BCC**
  - Multiple lesions may be present
  - Can vary in size from a few millimeters to several centimeters in diameter
  - Misdiagnosed as eczema or psoriasis
  - Most common pattern seen in HIV infection
Basal Cell Carcinoma (BCC)

- **Nodular BCC**
  - Classic BCC comprising 50-80% of all BCCs
  - Waxy or skin-colored papules that may crust, ulcerate, or bleed
  - A rolled border is present on larger lesions (rodent ulcer)
  - The lesion gradually enlarges over months to years
Basal Cell Carcinoma (BCC)

- **Nodular BCC**
  - Can reach a large size and extend deeply
  - Most frequently found on the face (>80% on the head and neck)
  - Melanin pigment may be present, making it easily confused with a melanocytic lesion
Basal Cell Carcinoma (BCC)

- **Morpheaform BCC**
  - This type of BCC is indurated and ivory in color
  - Atrophic with telangiectasias
  - May resemble scar or morphea
Basal Cell Carcinoma (BCC)

- **Infiltrative BCC**
  - Aggressive type of BCC characterized by deep infiltration into the dermis, subclinical spread, and high recurrence rate
  - 30% of all primary BCCs fall into this category
  - Ill-defined clinical margins
Basal Cell Carcinoma (BCC)

**Treatment**

- Depends on the type and aggressiveness of the tumor, patient age, patient sex, and site of the lesion
- A biopsy should be performed in all cases to determine the histologic subtype
- Aim of treatment is total removal or destruction with best cosmetic results
Basal Cell Carcinoma (BCC)

Treatment Options

- Excision
- Mohs micrographic surgery
- Curettage and electrodessication
- Radiation treatment
- Cryosurgery

- Lasers
- Photodynamic therapy
- Immune response modifiers
- Topical chemotherapy
- Systemic hedgehog inhibitors

Bullous Pemphigoid
Bullous Pemphigoid (BP) is a chronic autoimmune bullous disorder most commonly seen in the elderly population. It can occur in young children as well.

Originally described by Lever in 1953.

Most common autoimmune bullous disease in the Western Hemisphere.

6-7 cases/million population per year.
Bullous Pemphigoid (BP)

- BP is characterized by large, tense bullae in a generalized distribution with a predilection for flexural areas.
- Once the bullae rupture, large denuded patches are seen
- In the early course of the disease, pruritic patches and plaques may be seen with no bullous lesions
- Urticarial lesions and targetoid lesions can be seen
- Incidence of oral involvement is about 20%
Bullous Pemphigoid (BP)

- Blister formation results from antibodies directed against the hemidesmososomal antigens
  - BP Ag1 230 (230 kD)
  - BP Ag2 180 (180 kD)
- The antibody to BP Ag2 is the primary pathogenic factor
Bullous Pemphigoid (BP)

- Blister formation occurs due to:
  - Complement activation
  - Mast cells
  - Eosinophils
  - Neutrophils
Bullous Pemphigoid (BP)

- Histology reveals a subepidermal blister with a mixed inflammatory infiltrate mostly comprised of eosinophils.
- Direct immunofluorescence (DIF) demonstrates linear deposition of IgG and complement (C3) along the basement membrane zone (BMZ).
- Indirect immunofluorescence (IIF) on salt-split skin is also helpful.
- DIF is more sensitive than IIF.
Eosinophil-rich subepidermal blister with a smooth epidermal undersurface consistent with bullous pemphigoid
Direct immunofluorescence: linear deposition of IgG and C3 along the basement membrane zone
Indirect immunofluorescence: circulating IgG anti-basement membrane antibodies binding only to epidermal side of salt split skin with a titer of 1:80
Bullous Pemphigoid (BP)

- Must differentiate between BP and epidermolysis bullosa acquisita (EBA)
- Type IV collagen mapping localizes to the roof of the blister in EBA but to the base of the blister in BP
Bullous Pemphigoid (BP)

- BP has several subtypes which have been classified into primary cutaneous and mucosal variants and into generalized and localized forms.

- Localized BP is a rare variant of bullous pemphigoid which is classified into two types:
  1. Brunsting and Perry type
     - Characterized by scarring lesions of the head and neck
  2. Localized cutaneous non-scarring bullous pemphigoid (Eberhartinger and Niebauer type)
     - Characterized by non-scarring, bullous lesions of the extremities, especially the pretibial region.
     - This variant may also be present at other sites including forearms, chest, buttocks, and umbilicus
Bullous Pemphigoid (BP)

- Other variants of BP
  - Vesicular pemphigoid
  - Pemphigod nodularis
  - Pemphigoid vegetans
  - Erythrodermic pemphigoid
  - Non-bullous variant
Bullous Pemphigoid (BP)

**Treatment**

- Few controlled trials on BP
- Treatment depends on extent of disease on time of diagnosis and progression of disease
- High-potency glucocorticoids are the mainstay of treatment for localized disease
- Systemic glucocorticoids are most beneficial for generalized disease with the addition of a steroid sparing agent
Bullous Pemphigoid (BP)

**Treatment**

- Steroid sparing agents are added to avoid long-term corticosteroid use
- Mycophenolate mofetil, tetracycline and niacinamide, dapsone, erythromycin, methotrexate, cyclosporine, cyclophosphamide, chlorambucil and IVIG have been used
Bullous Pemphigoid (BP)

- **Course**
  - BP runs its course over 5-6 years
  - Relapses can be seen in 15% of patients
Bullous Pemphigoid (BP)

- **Course**
  - BP runs its course over 5-6 years
  - Relapses can be seen in 15% of patients
Rosacea
Rosacea

- Rosacea is a common inflammatory skin disease that affects the central facial skin
- Chronic inflammatory skin disorder that includes transient and permanent erythema, inflammatory papules and pustules, phymatous changes, and ocular symptoms
- Pathophysiology is multifactorial and an altered innate immune response is thought to be involved in this disease
- Complex disease with involvement of the neural, immune, and vascular pathways
Rosacea

Clinical features of rosacea include:

- Papules and or/pustules
- Flushing
- Skin sensitivity
- Burning or stinging
- Erythematous plaques
- Facial dryness
- Scaling
- Edema
Rosacea

- Four subtypes recognized by the National Rosacea Society
  1. Erythematotelangiectatic
  2. Papulo-pustular
  3. Phymatous
  4. Ocular
The National Rosacea Society Expert Committee (NRSEC) designated that patients may present with features that encompass more than one single rosacea subtype.
Rosacea

Subtype 1: Erythematotelangiectatic rosacea

- Flushing and persistent central facial erythema
- Telangiectases
- Highly sensitive cosmetically intolerant skin
- Must be distinguished from other inflammatory conditions such as chronic actinic damage and connective tissue disease
Rosacea

Subtype 2: Papulopustular rosacea

- Persistent central facial erythema
- Transient papules and pustules
- Absence of comedones and truncal lesions
- Older age group
- Must be distinguished from acne vulgaris, seborrheic dermatitis, perioral dermatitis, folliculitis and demodicidosis
Rosacea

Subtype 3: Phymatous rosacea

- Thickened skin
- Nodules
- Localized enlargement
- Firm induration of the skin secondary to fibrosis
- Rare variants such as granulomatous rosacea must be distinguished from other conditions such as sarcoidosis
Rosacea

Subtype 4: Ocular rosacea

- Bloodshot appearance
- Foreign body sensation
- Burning
- Stinging
- Light sensitivity
- Blepharitis
- Conjunctivitis
- Chalazions, hordeolum, and corneal complications
Rosacea

- Hallmark of rosacea is persistent central facial erythema mostly affecting the convex surfaces
  - Cheeks
  - Chin
  - Forehead
  - Nose
  - Sparing of the periocular and perioral areas
Rosacea

- In patients with darker skin type, the diagnosis of rosacea can be missed or delayed
- Features in darker skin type may include
  - Burning/stinging
  - Dryness
  - Edema
  - Sensitive skin
  - Sensation of flushing
Rosacea

- Ranges from 1%-20%
  - Rosacea affects an estimated 16 million Americans
- Distribution of rosacea is reported as equal or female predominant.
- Risk factors include:
  - Age
  - Phototype
  - Gender
  - Alcohol consumption
  - Genetic makeup
  - UV exposure
Rosacea

- Infectious Organisms Associated with Rosacea
  - Demodex
  - *Staphylococcus epidermidis*
  - *H. pylori*
Rosacea

- **Pathophysiology**
  - Complex
  - Genetic component
  - Interplay of adaptive and innate immune system
  - AMP
  - Antimicrobial peptides secreted by the keratinocytes in response to a microbial challenge
  - Eccrine glands, mast cells, and sebocytes are capable of producing AMP as well
Rosacea

- Defensins and Cathelicidins are AMPs in human skin
- α and β defensins are gene encoded
- Cathelicidin AMP (CAMP) is a cathelicidin gene identified in humans
- Increased levels of cathelicidins and protease activity are seen in patients with rosacea
- Mechanism is not fully understood
- Different signaling pathways including retinoid, Vitamin D, and cytokine-activated cascades are involved
Rosacea

Therapy

- Rosacea negatively impacts the quality of life of affected individuals
- Patients with rosacea can experience embarrassment, stress, social phobia, lack of confidence, and depression
### Summary of frequently used treatments of rosacea by subtype

<table>
<thead>
<tr>
<th>Subtype</th>
<th>Treatment options</th>
</tr>
</thead>
</table>
| Erythematotelangiectatic | Laser and intense pulsed light  
                        | Brimonidine tartrate                                                   |
| Papulopustular     | Metronidazole (topical)                                                 |
                        | Azelaic acid (topical)                                                  |
                        | Sulfacetamide sulfur (topical)                                          |
                        | Tetracyclines–tetacycline, doxycycline, minocycline (oral)              |
                        | Isotretinoin (for refractory cases)                                     |
| Ocular             | Antibiotics–azithromycin, erythromycin, bacitracin (topical); tetracyclines, metronidazole (oral) |
                        | Corticosteroids–rimexolone, loteprednol                                  |
                        | Cyclosporine (topical)                                                  |
| Phymatous          | Isotretinoin                                                            |
                        | Laser ablation                                                          |
                        | Surgery                                                                 |

Rosacea

**Therapy**

- Subantimicrobial-dose cyclines
- The anti-inflammatory effects of tetracyclines led to the development of subantimicrobial dose doxycycline (SDD)
- Thought to act by various mechanisms
- ↓ activity of kallikrein 5 enzyme which in turn
- ↓ Cathelicidins
Rosacea

- **Therapy**
  - β-blockers
  - Oral ivermectin
Rosacea

- **New topical therapy**
  - Brimonidine tartrate gel 0.33%
    - α-2 adrenergic agonist that causes peripheral vasoconstriction of smooth muscle receptors
    - First drug approved to treat facial erythema of rosacea
  - Ivermectin
    - Anti-inflammatory and acaricidal properties against Demodex
  - Oxymetazoline
Rosacea

- Ivermectin 1% cream
  - Two 40-week extension studies were conducted to assess the long term safety of ivermectin 1% cream vs azelaic acid 15% gel
  - Lower incidence of adverse events in the ivermectin group compared to azelaic acid group
  - Safe and effective for up to 52 weeks

Long-Term Safety of Ivermectin 1% Gel in Treating Inflammatory Results of Two 40-Week Controlled, Stein Gold et al, Journal of Drugs in Dermatology, Nov. 2014, Vol 13, issue 11
Rosacea

Baseline
IGA= 4; Lesion count = 63

Week 12
IGA= 1; Lesion count = 2

Data on file. Fort Worth, TX; Galderma Laboratories, L.P.
Rosacea

▶ Therapy

▶ Vascular Lasers
  ▶ Pulse dye laser (PDL, 585-595nm)
  ▶ Potassium-titanyl-phosphate laser (KTP, 532nm)
  ▶ Diode-pumped frequency doubled laser (532nm)
  ▶ Neodymium-doped yttrium aluminium garnet laser (Nd:YAG, 1064nm)
Rosacea

Courtsey: Syneron Candela Corp.
Rosacea

Summary

- Chronic condition with no cure
- Exact cause is unknown
- Dysregulation of the immune system as well as neurovascular system
- Adversely affects the quality of life
- Identification of trigger factors
- Cosmetic intolerance and increased sensitivity of skin are common features
- Use of gentle, broad spectrum sunscreens, avoidance of extended sun exposure and use of non irritating cosmetics is recommended
- Therapy should be tailored to the predominant clinical subtype to optimize therapy
References


Dermatomyositis
Dermatomyositis (DM)

- Dermatomyositis (DM) is a condition that is characterized by an inflammatory myopathy with characteristic cutaneous findings.
- It is a systemic disorder that most commonly affects the skin and muscles but can also affect the joints, muscles, esophagus, and occasionally the heart.
- DM with subclinical or absent myopathy is called amyopathic dermatomyositis.
Dermatomyositis (DM)

Cutaneous Manifestations of Dermatomyositis

- The disease begins with erythema and edema of the face including the eyelids
- Gottron’s papules
  - Flat topped, polygonal violaceous papules over the knuckles
- Heliotrope eruption
- Violaceous erythema over the eyelids
- Psoriasiform dermatitis of the scalp
Heliotrope
Cutaneous Manifestations of Dermatomyositis

- Gottron’s sign
  - Erythematous, atrophic, scaly patches on the MCPs, elbows, and knees
- Shawl sign
  - Erythema with or without poikiloderma on the shoulders and upper back
- V-neck-sign
  - Erythematous patches on the chest in a V-shaped distribution
- Flagellate erythema
- Prominent telangiectatic vessels of the proximal nail fold with cuticular hypertrophy
Dermatomyositis (DM)

Muscle disease may occur simultaneously, precede or follow the skin symptoms

- Symmetric proximal muscles weakness mostly involving the shoulder girdle and occasionally the pelvis region
- Muscle weakness can be noted on climbing stairs, combing hair, or rising from a chair
Dermatomyositis (DM)

Systemic Manifestations

- Weight loss
- Fever
- Arthralgia
- Dysphonia
- Dysphagia
- Gastroesophageal reflux
- Dyspnea
Dermatomyositis (DM)

**Laboratory Evaluation**

- Muscle enzymes
  - Creatine kinase (CK)
  - Aldolase
  - Aspartate aminotransferase (AST)
  - Lactic dehydrogenase (LD)
- Antinuclear antibodies
- Myositis-specific antibodies
- Electrocardiography
- Esophageal manometry
- Colonoscopy
- Papanicolaou smear
- CA-125 and CA-19-9
- Pulmonary function tests
Dermatomyositis (DM)

Imaging studies

- MRI
- CT scanning of chest, abdomen, and pelvis
- Transvaginal ultrasound and mammography
- Barium swallow
Dermatomyositis (DM)

Histopathology

- Histology reveals thinning of the epidermis, subtle interface vacuolar infiltrate, not significant increased basement membrane thinning or dyskeratosis and significantly increased dermal mucin

- Direct Immunofluorescence: Cutaneous DIF is positive in at least 90% of patients

- Cytoid bodies, continuous granular staining with C5b-9, stronger than C3, and focal granular IgG and IgM along the basement membrane
Dermatomyositis (DM)

Management

- Occult malignancy is seen in up to one-third of the patients
- Colon
- Breast
- Pancreatic
- Ovarian
- Lymphoma
Dermatomyositis (DM)

Treatment

- **Corticosteroids**
  - Prednisone is first-line therapy
- **Immune globulins**
- **Antimalarial agents**
  - Hydroxychloroquine
  - Chloroquine

- **Corticosteroid sparing immunosuppressants**
  - Methotrexate
  - Azathioprine
  - Mycophenolate mofetil
  - Sirolimus
  - Cyclosporine
  - Tacrolimus
References

Thank you