Pediatric Dermatology:
Tumors of Fat, Muscle and Bone;
Epidermal, Appendageal and Dermal Tumors

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Disclosure

- I have no actual or potential conflict of interest in relation to this presentation
Objectives

• 1. Tumors of Fat
• 2. Tumors of Smooth Muscle
• 3. Tumors of Skeletal muscle
• 4. Histiocytic Neoplasms
• 5. Tumors of Bone
• 6. Appendageal tumors
• 7. Neural tumors
• 8. Fibrohistiocytic Tumors
Benign Tumors of Fat: Lipoma

• Epidemiology
  – Most common benign tumor of fat
  – Any age; more common during or after puberty

• Clinical Presentation
  – Asymptomatic; soft, subcutaneous nodule

• Associated with
  – Bannayan-Riley-Ruvalcalba
  – Gardner’s syndrome
  – Proteus syndrome
  – MEN1
  – Familial multiple lipomatosis
  – Dercum’s disease
  – Madelung’s disease
  – CLOVE syndrome

• Treatment
  – Observation or Excision
Lipoma

Lobulated proliferation of mature adipocytes
Angiolipoma

- Epidemiology
  - Lipoma variant
  - Clinically indistinguishable except they tend to be painful, greater tendency to be multiple
  - Primarily in teenagers and young adults
- Clinical Presentation
  - Commonly present on upper extremities and trunk
- Treatment
  - Excision
Angiolipoma

- Vascular proliferation
- Adipocyte
- Thrombi
Spindle Cell

- Epidemiology
  - Majority found in middle-aged to older men
- Clinical Presentation
  - Usually presents as a solitary, slow growing, mobile, painless subcutaneous nodule without epidermal change
  - Upper back and posterior neck
- Treatment
  - Excision
Spindle cell lipoma
Spindle cell lipoma
Myxoid lipoma
Pleomorphic lipoma - Floret cells
• Spindle cell, myxoid & pleomorphic lipoma - exist as a morphologic continuum
• Monosomy or partial loss of chromosomes 13 and 16 are the most common alterations seen in spindle cell, pleomorphic and myxoid lipoma
Hibernoma

- Epidemiology
  - Rare, benign tumor that is derived from brown fat
  - Young adults in their twenties and thirties
- Clinical Presentation
  - Interscapular area, thighs, shoulder, neck, chest, arms and abdominal cavity/retroperitoneum
  - Hibernomas are slow-growing tumors located in the subcutis or, occasionally, within skeletal muscle
- Treatment
  - Surgical excision is curative
  - May be difficult to excise as they often are in close proximity to neurovascular structures
Nevus Lipomatosus Superficialis

Epidemiology
- Rare hamartoma develops shortly after birth or during the first two decades of life

Clinical Presentation
- Grouped, soft papulonodules
- Most commonly located on the buttocks or upper thighs

Treatment
- Excision
Malignant Tumors of Fat

- Well differentiated Liposarcoma/Atypical Lipomatous tumor
- Myxoid Liposarcoma
- Round cell Liposarcoma
- Dedifferentiated Liposarcoma

- They are very rare in kids and very rare in the skin
- They are mostly deep seated tumors in the subcutaneous locations (the most common location being in the retro peritoneum)
- Very rarely encountered in a dermatology
- For boards need to remember the translocation encountered in *Myxoid Liposarcoma* (t(12;16)(EWSR1;DDIT3))
Leiomyomas

Epidemiology

- Benign tumors derived from cutaneous smooth muscle
- Majority of these lesions arise from arrector pili muscles, the media of blood vessels

Clinical Presentation

- Solitary or multiple
- Pink, red, or dusky brown, firm dermal nodules of varying size
- Subject to episodes of paroxysmal spontaneous pain
- Common locations include back, face, extensor surfaces of the extremities and usually arranged in groups

- Multiple leiomyomas may be associated with Reed syndrome aka Hereditary leiomyomasis and renal cell cancer syndrome
  - Autosomal dominant mutation in fumarate hydratase

Treatment

- Excision
Pilar leiomyoma

Cross section with round nuclei and vacuoles

Longitudinal section with "cigar" nuclei
HLRCC (Hereditary leiomyomatosis renal cell carcinoma syndrome)

- *Multiple* cutaneous & uterine leiomyomas
- *Renal cell carcinoma* (papillary or collecting duct renal cell carcinoma)
- *Autosomal dominant disorder*
- Loss of function of tumor suppressor gene- *Fumarate hydratase (FH)(1q42.3~q43)*, resulting in fumarate hydratase deficiency
Leiomyosarcoma

- Epidemiology
  - Rare soft-tissue sarcoma, occurs primarily in adults, more common in males
  - Superficial (Cutaneous) leiomyosarcomas are limited to the dermis
    - favorable prognosis, can recur, but very rarely metastasize
  - Subcutaneous leiomyosarcomas that primarily arise in or extensively involve the subcutis
    - Metastasize in approximately 25–40% of cases, with a mortality rate of between 30% - 50%

- Clinical Presentation
  - Solitary, deeply seated, firm nodules, with variable associated erythema and hyperpigmentation
  - Can arise anywhere on the body, more common the extensor surfaces of the extremities
Prognostic Factors in Leiomyosarcoma

- The subcutaneous location &
- Tumor size >5 cm

- Are associated with aggressiveness

- Treatment
  - Wide excision with meticulous examination of all surgical margins
Rhabdomyosarcoma

Epidemiology

- Rhabdomyosarcoma is the most common soft-tissue sarcoma in children and adolescents
- Usually arise from the deep soft tissues, dermal origin is rare
- Malignant soft-tissue neoplasm of skeletal muscle origin
- 3 histological types: Alveolar, Embryonal and Pleomorphic
- Alveolar most common type in the skin
- Tends to display aggressive behavior in both adults and children

Clinical Presentation

- Presents as an asymptomatic mass on the head and neck, especially the nasal cavity and paranasal sinuses
- As the tumor grows, pain and swelling become the most common symptoms

Treatment

- Surgery, radiotherapy and chemotherapy
Alveolar Rhabdomyosarcoma

\( T(2;13) \) resulting in PAX3-FKHR fusion is seen in Alveolar Rhabdomyosarcoma
Benign Bone Tumors: Bone-forming tumors
Osteoid Osteoma and Osteoblastoma

**Epidemiology**
- Both tumors are typically seen in the second decade of life
- More common in males

**Pathology**
- Resemble each other, with increased osteoid tissue formation surrounded by vascular fibrous stroma and perilesional sclerosis

**Osteoid Osteoma**
- **Clinical Presentation**
  - Smaller lesions that occur in the cortex of long bones
  - Presents with nocturnal pain
  - Multiple seen in **Gardner Syndrome**
- **Treatment**
  - NSAIDs for pain relief
  - Excision; do not tend to recur

**Osteoblastoma**
- **Clinical Presentation**
  - Bigger lesions; most frequently in the axial skeleton
  - Pain but not worse at night
- **Treatment**
  - Higher rate of recurrence
Epidemiology

- Most common malignant tumors of bone in pediatric population
  - Second most common is Ewing’s sarcoma
- Associated dermatologic disorders:
  - Rothmund-Thompson syndrome (AR, RECQL4, photosensitive genodermatosis, poikiloderma, hypoplastic thumbs)
  - Li-Fraumeni syndrome (AD, P53 mutation, multiple malignancies)
  - Bloom syndrome (AR, RECQL2, RECQL3, photosensitive, decreased IgM)
  - Neutrophilic eccrine hidradenitis
Histiocytic Neoplasms

**Langerhans Cell-Derived**
- Langerhans Cell Histiocytosis/Histiocytosis X
- Congenital Self Healing Reticulohistiocytosis/CSHR (Hashimoto Pritzker disease)

**Non-Langerhans Cell Histiocytosis/Histiocytic Neoplasms**
- JXG/Xanthogranuloma
- Clinical & Histologic variants of JXG.
Langerhans Cell Histiocytosis

• Epidemiology
  – Can occur at any age
  – Peak incidence between 1 and 4 years of age
• Clinical Presentation
  – Older classification system
    • Eosinophilic granuloma (Localized bone disease)
    • Hand-Schuller-Christian disease (Skull lesions, exophthalmos, diabetes insipidus)
    • Letterer-Siwe disease (Acute or subacute disseminated form)
  – Modern classification-LCH is an umbrella term with notation made for various organs involved

• Clinical Presentation
  – Most common clinical presentation in kids: Seborrheic dermatitis-like reaction (Scalp, posterior auricular regions, perineum, axillae)
  – Erythematous, red-brown papules, secondary erosion, hemorrhage, or crusting
  – In neonates, vesiculopustular lesions can be seen
  – Can have mucosal involvement
  – Bone lesions are common (most commonly skull “Punched-out” appearance)
• Treatment
  – Depends on the extent of the disease
  – Topical treatments for localized disease include steroids and Nitrogen mustard
  – Systemic disease treated with chemotherapy (Vinblastine or Etoposide)
IHC

- Langerhans histiocytes are:
  - CD1a++
  - S100+
  - Langerin+ (CD 207)
EM shows numerous intracytoplasmic Birbeck Granules
Juvenile Xanthogranuloma

• Epidemiology
  – Common form of non-LCH
  – Benign, self-limited disease of infants, children, and sometimes adults
  – Systemic involvement is very rare

• Clinical Presentation
  – Firm, round papule or nodule of varying size
  – Early lesions are erythematous to orange or tan
  – Mature lesions are yellow in color
  – Most often solitary, can be multiple
  – Head, neck, and trunk are the most common location
  – **Eye is the most common extracutaneous organ involved (iris is the site most often involved)**
  – Potential complications: hyphema, glaucoma, blindness
  – Need ophthalmology referral

• Important association
  – Juvenile chronic myelogenous leukemia (JCML)
  – Neurofibromatosis type 1

• Treatment
  – No treatment necessary for solitary lesions
  – Systemic disease treated with Chemotherapy similar to LCH
Juvenile Xanthogranuloma
Other “Non-Langerhans Cell” Histiocytic Neoplasms
(Clinical & Histologic Variants Of JXG/XG)

- Spindle cell Xanthogranuloma
- Progressive Nodular Histiocytosis
- Generalized Eruptive Histiocytoma
- Benign Cephalic Histiocytosis
- Papular Xanthoma
- Xanthoma Disseminatum
- Scalloped Cell Xanthogranuloma
Epidermal Nevus

- Epidemiology
  - Benign congenital lesions characterized by hyperplasia of epidermal structures
  - Usually present at birth
  - Affects both sexes equally

- Clinical Presentation
  - Often favor the extremities, but may occur anywhere
  - Blaschko’s distribution: linear on extremities, arcuate or wavy on trunk

- Treatment
  - Challenging; Superficial destructive therapies lead to high recurrence rate
  - Cryotherapy, dermabrasion, electrodesiccation, CO2 laser ablation
  - Topical therapies have variable results
    - Retinoids, 5-FU, steroids
  - Full-thickness surgical excision are effective for smaller, localized lesions
Epidermal Nevus Syndromes

- 5 well-defined epidermal nevus syndromes:
  - Schimmelpenning syndrome
  - Nevus comedonicus syndrome
  - Pigmented hairy epidermal nevus syndrome
  - Proteus Syndrome
  - CHILD

- Biopsy should be performed to check for Epidermolytic Hyperkeratosis (EHK)
  - These patients can transmit these mutations to offspring

- Extracutaneous abnormalities seen in patients with ENS include:
  - Seizures, Mental retardation, Hemiparesis
  - Cranial nerve palsies, Developmental Delay
  - Kyphosis/Scoliosis, Limp hypertrophy
  - Macrocephaly, Colobomas
  - Corneal/Retinal changes, Cataracts
  - Cardiac and GU defects
Epidermolytic Hyperkeratosis
Inflammatory Linear Verrucous Epidermal Nevus

• Epidemiology
  – Unique variant of epidermal nevus
  – Often present at birth or appear during early childhood

• Clinical Presentation
  – Most often on an extremity
  – Presents as erythematous, pruritic scaly, verrucous papules the coalesce into linear plaques

• Treatment
  – Topical or intalesional steroids may help with pruritus and reduce inflammation
  – Similar to epidermal nevus treatments
Inflammatory linear verrucous Epidermal nevus (ILVEN)

Alternating hyper & parakeratosis with psoriasiform acanthosis
Nevus Sebaceous of Jadasson

- Epidemiology
  - Common congenital lesion accruing mainly on face and scalp
  - Generally present at birth, but may be noted during early childhood or rarely adult life

- Clinical Presentation
  - well-circumscribed, hairless, yellow-orange to tan plaque
  - Multiple nevi sebaceous may occur in association with *Schimmelpenning syndrome*
Nevus Sebaceous of Jadasson

- Treatment
  - Surgical excision has been recommended traditionally out of concern for development of secondary neoplasms
    - Most common secondary benign neoplasm is SPAP
    - The most common secondary malignant neoplasm is BCC
    - Most of them are probably trichoblastomas
Apocrine glands are not normally found in the scalp; but occur in a “nevus sebaceus” as the lesion matures.
Tumors of the Epidermal Appendages
Trichofolliculoma

- Epidemiology
  - Benign appendageal neoplasm of hair follicle derivation
  - Usually occurs as a solitary lesion on head and neck of adults, but may occur during childhood

- Clinical Presentation
  - 2-10mm, slow-growing, flesh-colored papule or nodule with a smooth surface
  - Often a central pore with a protruding tuft of hair

- Treatment
  - Surgical excision
Trichofolliculoma

Small mature follicles
Comedo
Fibrotic stroma
Vellus hairs
Trichohyalin
Pilomatricoma

• AKA Calcifying Epithelioma of Malherbe or Pilomatrixoma

• Epidemiology
  – Benign tumor derived from hair matrix
  – Usually present as a solitary lesion on the face, neck, upper trunk, or upper extremities
  – Usually develops within first two decades of life
Pilomatricoma

- Clinical Presentation
  - Flesh-colored to white, firm papules or papulonodules
  - May have overlying pink to blue hue
  - Generally very hard, due to calcifications

- Multiple pilomatricomas have been noted in patients
  - Myotonic Dystrophy
  - Gardner syndrome
  - Rubinstein-Taybi syndrome
  - Trisomy 9
Pilomatricoma
Trichoepithelioma

• Epidemiology
  – Occur as solitary nonhereditary tumor seen in early adult life or occasionally during childhood
  – Multiple small lesions occurring primarily on the face inherited in an autosomal dominant fashion: **Brook-Spiegler Syndrome**
    • Begin during early childhood or around puberty as small, firm, flesh-colored papules
• Other associations include
  – **Rombo**- (Trichoeps + BCCs, milia, atrophoderma vermiculatum, hypotrichosis)
  – **Rasmussen**- (Trichoeps + cylindromas + milia)

• Clinical Presentation
  – Distributed mainly on the face, nose, nasolabial folds, forehead, upper lip, eyelids and occasionally scalp

• Treatment
  – Can be difficult when multiple lesions are present
  – Single lesions can be treated with surgical excision, ED&C, or laser therapy
Trichoepithelioma
Trichilemoma / Trichilemmal verruca

• Epidemiology
  – Benign appendageal neoplasm derived from hair follicle
  – Predominantly occur in adults, can be seen in kids
  – Equally common in males and females

• Clinical Presentation
  – Can be solitary or multiple flesh-colored papules, occasionally with verrucous surface
  – Most common on head and neck
  – Multiple trichilemmomas may be seen in the setting of Multiple Hamartoma syndrome or Cowden disease

• Treatment
  – Can be difficult when multiple
  – Single lesions can be surgically excised
Trichilemmoma/Trichilemmal verruca

- Hyperkeratosis
- Lobule of clear cells
- Thin rim of basaloïd cells

- Clear cells
- Thin rim of basaloïd cells
- Thick basement membrane
Multiple Hamartoma Syndrome (Cowden disease)

• AD
• Characterized by hamartomas of multiple organ systems
• Mucocutaneous lesions include trichilemmomas, palmoplantar keratosis, oral papillomatosis, sclerotic fibromas
• Extracutaneous manifestations include fibrocystic breast disease, breast fibroadenomas, thyroid adenomas, meningiomas, and intestinal polyposis
• Increased risk of breast cancer, endometrial cancer, cancer of GI tract and thyroid gland
Syringoma

- Epidemiology
  - Can occur at any age, but frequently present initially during puberty
  - Seen in increased frequency in patients with Down Syndrome
- Clinical Presentation
  - Benign tumors of eccrine glands
  - May occur as isolated or multiple lesions
  - Small, firm, flesh-colored to yellow, translucent papules
  - Most common location is the eyelids, but can be seen on neck, torso, extremities and genitalia

- Treatment
  - Can be difficult for multiple lesion
  - Cryosurgery, desiccation, CO2 lasers have all been used
Syringoma

- Horn cyst
- Fibrosis
- Duct within "tadpole"
Cylindroma

- Clinical Presentation
  - Also known as turban tumors
  - Benign tumor of either eccrine or apocrine glands
  - Firm, rubbery, pink to bluish plaques or nodules
  - Located primarily on the scalp, occasionally on the face, trunk, or extremities
  - Multiple lesions may occur as part of Brook-Spiegler Syndrome (CYLD gene mutation, 16q12-13)

- Treatment
  - Surgical excision, although CO2 laser surgery been used with some success
Cylindroma

- Fibrosis
- Sweat ducts
- Jigsaw puzzle of basaloid cells
- Hyalinized cylinder
- Basaloid cells
- Hyalinized droplets
Angiofibroma

• Epidemiology
  – May occur as isolated or multiple lesions
  – Multiple facial angiofibromas are commonly seen in patients with **tuberous sclerosis** (adenoma sebaceum), **MEN type 1**, and **Birt-Hogg-Dube syndrome**

• Clinical Presentation
  – Clinical subtypes include fibrous papules, pearly penile papules and periungual fibromas
  – Angiofibromas present as flesh-colored shiny papules
  – Periungual fibromas present as flesh-colored filiform growths of proximal nail fold, multiple lesions are **pathognomonic for tuberous sclerosis**

• Treatment
  – Solitary lesions can be treated with shave excision or electrocautery
  – Pearly penile papules do not require treatment
  – Multiple lesions of Tuberous Sclerosis can be treated with **Rapamycin (Sirolimus)**—an mTOR inhibitor
Angiofibroma (Fibrous papule)

- Dilated vessel
- Dense perpendicular collagen
- Small dome-shaped papule
Neurofibroma

- Epidemiology
  - Sporadic in healthy individuals
  - Cutaneous marker of **Neurofibromatosis type 1**
  - Neurofibromas are benign tumors composed of neuromesenchymal tissue, including Schwann cells, endoneurial and perineurial cells
  - Often present during young adulthood or childhood
- Clinical Presentation
  - Soft, flesh-colored papules or papulonodule
  - Exhibit a positive “buttonhole” sign
  - When multiple neurofibromas are present, the diagnosis of NF1 must be considered
  - Plexiform neurofibroma present as a large, lobulated nodular plaque, may have a “bag of worms” consistency on palpation
    - Pathognomonic for NF1
- Treatment
  - Excision can be used
  - Electrodessication for smaller lesions
  - Can be difficult when multiple
Neurofibroma

- Spindle cell proliferation
- Bubblegum pink stroma
- Sweat duct
- Mast cell
- Wavy spindle cells
Malignant Peripheral Nerve Sheath Tumor

- Malignant counterpart of neurofibroma
- Rare cutaneous tumor
- Mostly seen in patients with Neurofibromatosis type 1, developing in a preexisting Neurofibroma
Dermatofibroma (fibrous histiocytoma)

• Epidemiology
  – Benign neoplasm of connective tissue
  – Only occasionally seen in children

• Clinical Presentation
  – Small, well-defined dermal nodule
  – Tan to brown color
  – Can be found anywhere
  – Most common on extremities
  – “Dimple sign”—useful diagnostic feature

• Treatment
  – No treatment is necessary
  – Can be excised
Inclusion Body Fibromatosis/Infantile digital fibroma

• Epidemiology
  – Infants under 1 year of age
  – Boys and girls are equally affected

• Clinical Presentation
  – Firm, smooth, skin-colored, dome-shaped nodules on the dorsolateral aspects of the fingers and toes

• Treatment
  – Spontaneous regression within 2–3 years is the usual natural history
  – Conservative observation, if small, to wide local excision if large or compromises function
  – High local recurrence rates
Fibrous Hemartoma of Infancy

• Epidemiology
  – Rare, benign soft tissue tumor
  – Usually presents before 2 years of age
  – More common in boys

• Clinical Presentation
  – Most common locations are upper trunk, axillae, upper extremities
  – Painless, flesh-colored subcutaneous nodule or plaque
  – Most cases are solitary
  – Slow growing

• Treatment
  – Full surgical excision
CD 34 positive and can be confused with DFSP
Dermatofibrosarcoma Protuberans

• Epidemiology
  – Seen mostly in adults (second and fifth decade)
  – Pediatric and even congenital cases are rarely seen

• Clinical Presentation
  – Erythematous to blue papules and nodules
  – Increase in size and become multinodular and protuberant
  – Some lesions present as atrophic plaques
  – Trunk and proximal extremities are most common locations

• Pathology
  – Chromosomal translocation t(17;22) COL1A1 and PDGFb genes

• Treatment
  – Complete excision
  – MMS has been used in both pediatric and adult cases
  – Radiation and Imatinib has been used if clear margins could not be abstained
References


