Vascular Tumors - In Medusa’s Image

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Capillary Hemangioma

- One of the most common benign orbital tumors of infancy
- Typically absent at birth and characteristically have rapid growth in infancy with later spontaneous involution
- Distinguish from vascular malformations
  - Present at birth
  - Very slow growth with persistence into adult life
- About 50% in head and neck region
- 30% at birth
- 100% by age 6 months
Pathophysiology

- Hamartomatous proliferations of vascular endothelial cells
- Proliferative phase
  - From 8-18 months
  - Increased endothelial and mast cells
- Involutional phase
  - 50% involute by age 5 years
  - 70% involute by age 7 years
  - Mast cell numbers decrease to normal and there is a decrease in endothelial and mast cell activity
Syndromes

- **Kasabach-Merritt syndrome**
  - Mortality rates from 30-50%
  - Consumption coagulopathy and thrombocytopenia secondary to platelet sequestration
  - Disseminated intravascular coagulation
  - High-output congestive heart failure

- **Ophthalmic morbidity**
  - Space-occupying effects
  - Deprivation amblyopia in the affected eye if the lesion is large enough to directly occlude the visual axis
  - Anisometropic amblyopia if corneal distortion and astigmatism occur
Treatment

■ Observation!

■ Corticosteroids
  ■ Topical steroid formulations for cutaneous lesions
  ■ Injectable steroid formulations also are used in the treatment of these lesions.
  ■ Systemic corticosteroids are used for amblyogenic life-threatening lesions.
    ■ Excellent response in 30% of patients, a questionable response in 40%.

■ Interferon alfa-2a
  ■ Preventing endothelial cell migration in capillary hemangiomas
  ■ Adverse effects include fever, chills, arthralgias, and retinal vasculopathy
  ■ Spastic diplegia in 20% in some reports
Treatment

- Laser surgery controversial
  - CO2 laser with hemostatic effects
  - Other lasers used include the argon laser and Nd:YAG laser
  - Pulsed dye laser is only effective for very superficial lesions; its mechanism of action is too slow

- Incisional surgical techniques variable success
  - Surgical ligation equivocal results
  - Vascular embolization for large extraorbital hemangiomas only
  - Primary excision advocated for infantile hemangiomas
Angiokeratoma

- Lower extremities as an asymptomatic solitary papule or plaque, elevated, warty, dark red to purple, slightly compressible papules.
- Rough hyperkeratotic scale is often found over the surface and the edges of these papules due to epithelial hyperplasia and hyperkeratosis
- Irregular borders and associated pigmentation, secondary to intraepidermal hemorrhage
- Sometimes, a linear distribution (with bands or streaks) of papules
- May present with epithelial erosion and bleeding
Angiokeratoma

- Clinical variants
  - Angiokeratoma circumscriptum (Angiokeratoma corporis neviform)
  - Angiokeratoma Mibelli-type on the fingers and the toes
  - Fabry’s disease (on a lower extremity or the trunk)
  - Angiokeratoma of Fordyce (found on the scrotum)
  - Caviar spots (angiokeratomas of the tongue)

- Clinical associations
  - Cobb syndrome
    - Klippel-Trenaunay syndrome
  - Nevus flammeus
  - Cavernous hemangiomas
  - Traumatic arteriovenous fistulas
Angiokeratoma

- Exophytic profile with numerous ectatic thin-walled vascular channels surrounded by epidermal collarette
- Thrombosis of these vessels is common
- Clinically may mimic melanoma
- Fabry disease—may contain cytoplasmic vacuoles in endothelial cells, fibroblasts, and pericytes
- Treatment
  - Usually no treatment
  - Surgical or laser removal
Pyogenic Granuloma
(Lobular capillary hemangioma)

- Smooth firm nodules with bright or dusky red color
- Solitary, well circumscribed, dome shaped, 1-10 mm in diameter
  Sessile or pedunculated
- Children
  - Head and neck (62.4%)
    Trunk (19.7%)
    Upper extremity (12.9%)
    Lower extremity (5.0%)
    Skin (88.2%)
- Pregnant women (Granuloma gravidarum)
  - Gingival mucosa
Pyogenic Granuloma

- Rapid growth, often with history of trauma
- Uncommon variants
  - PG with satellitosis
  - Intravenous PG
- Treatment
  - Removal by surgery or laser
Pyogenic Granuloma DDX

- Bacillary angiomatosis
  - Clinical history
  - Neutrophils adjacent to the blood vessels
  - Granular material resembling fibrin
  - Warthin-Starry silver or GMS stain
Kaposi Sarcoma

- **Epidemic AIDS-related KS**
  - Most common presentation, with visceral involvement common
  - In the United States, KS serves as an AIDS-defining illness in 10-15% of HIV-infected homosexual men
  - In Africa and developing regions, epidemic AIDS-related KS is common in heterosexual adults and occurs less often in children.

- **Immunocompromised KS**
  - Following solid-organ transplantation or in patients receiving immunosuppressive therapy
  - Congenital immunodeficient states are not at increased risk for developing KS
  - Average time to development of KS following transplantation is 30 months
  - Visceral involvement is common

- **Classic KS**
  - Elderly men of Mediterranean and Eastern European background
  - Protracted and indolent course, visceral involvement uncommon
  - Common complications include venous stasis and lymphedema
  - 30% of patients may develop a second malignancy

- **Endemic African KS**
  - HIV seronegative in Africa and may carry an indolent or aggressive course
KS and HHV-8

- Originates from a single cell clone rather than a multifocal origin
- Human herpes virus 8 (HHV-8) genomic sequences have been identified by polymerase chain reaction in more than 90% of all types of KS lesions (including epidemic and endemic forms),
- Also associated with body cavity-based lymphomas, Castleman disease, and leiomyosarcomas that occur in individuals infected with HIV
Kaposi Sarcoma

- Cutaneous lesions any location but usually lower extremities and the head and neck region
- Palpable and nonpruritic, macular, papular, nodular, or plaquelike appearances
- Several millimeters to several centimeters in diameter
- Brown, pink, red, or violaceous color and may be difficult to distinguish in dark-skinned individuals
- Discrete or confluent
- Mucous membrane involvement is common (palate, gingiva, conjunctiva)
KS-Histopathology

- Proliferation of spindle cells, prominent slitlike vascular spaces, and extravasated red blood cells
- Hyaline globules, PAS positive
- Promontory sign in early lesions
Kaposi Sarcoma

- AIDS Clinical Trials Group (ACTG) proposed staging system
- **Good risk**
  - Tumor (T) - Confined to skin and/or lymph nodes and/or minimal oral disease
  - Immune system (I) - CD4 greater than 200/mm³
  - Systemic illness (S) - No history of opportunistic infection, more than 10% involuntary weight loss, or diarrhea persisting more than 2 weeks
  - Karnofsky performance status greater than 70
- **Poor risk**
  - Tumor (T) - Tumor-associated edema or ulceration, extensive oral KS, gastrointestinal KS, KS in other non-nodal viscera
  - Immune system (I) - CD4 less than 200/mm³
  - Systemic illness (S) - History of opportunistic infection, unexplained fever, night sweats, more than 10% involuntary weight loss, or other HIV-related illness (ie, lymphoma, neurologic disease)
  - Karnofsky performance status less than 70
KS-Treatment

- Antiretroviral therapy HAART
- Local therapy
  Best suited for individuals who require palliation of locally advanced symptomatic disease (e.g., radiation) or for individuals who have cosmetically unacceptable lesions
  - Radiation therapy
    - Most widely used and effective local therapy
    - Responses occur in 80-90% of patients
    - A higher cumulative dose (40 Gy) results in better local control than lower doses (8 Gy or 20 Gy).
    - Electron beam therapy is reserved for treatment of superficial lesions
  - Intraläsional vinblastine
  - Cryotherapy
  - Topical retinoids
    - Retinoic acid down-regulates IL-6 receptor expression, IL-6 critical for neovascularization
KS-Treatment

- Systemic therapy for extensive or symptomatic visceral disease, rapidly progressive mucocutaneous disease, and symptomatic lymphedema.

- Interferon-alfa
  - Time to clinical response is long (ie, 4 mo)
  - Most effective when the CD4 count is greater than 150-200/mL or when administered in conjunction with antiretroviral therapy

- Chemotherapy
  - Not used with curative intent
  - Indicated for symptomatic visceral or rapidly progressive mucocutaneous disease
  - FDA approved include liposomal doxorubicin (Doxil), liposomal daunorubicin (DaunoXome), and paclitaxel (Taxol)
Cutaneous Angiosarcoma

- Elderly males
- Head and neck
- Clinical features variable with enlarging bruise, cellulitis, edema, a blue-black nodule, or an unhealed ulceration
- Rarely angioneurotic edema and scarring alopecia
Angiosarcoma

- Low-grade lesions
  - Vascular spaces lined by large plump endothelial cells that penetrate the stroma and papillary fronds of cells that project into the lumen

- Higher-grade lesions
  - More cellular, with atypical cells and abnormal mitoses.

- IPOX
  - Vimentin and CD31
    - CD34 (74%)
    - Cytokeratins (35%)
Angiosarcoma

- Surgical treatment but contraindicated in tumors:
  - Extending into vital structures
  - Massive size
  - Multicentricity

- Primary excision of the scalp should be full-thickness, including the pericranium and, if indicated, the outer table of the cranial vault
  - Wide margins (at least 5 cm) on all sides

- Postoperative radiotherapy
  - Unsatisfactory margins
  - Large tumor size
  - Deep extension
  - Multicentricity

- Radical radiation therapy in the form of high-field electron beam therapy shows promise
Angiosarcoma

- Overall prognosis poor
- Median time of survival ranges from 15-24 months
  - 5-year survival rate of 12-33%
- Metastasis
  - Local failure and metastases to local cervical lymph nodes common
  - Lung is the most common site of distant metastasis, followed by the liver and bone
- Unfavorable Prognostic Variables
  - Tumor size (>5 cm)
    - Incomplete surgical resection
    - Minimal lymphoid infiltrate in and around the tumor
  - Unresectable lesions and metastatic disease at diagnosis
  - Delayed diagnosis and treatment
  - Grade is not useful in predicting survival
  - No correlation with appearance (eg, ulcerated, nodular, diffuse)
Glomus Tumor

- **Solitary glomus tumors**
  - Blue or purple, papules or nodules that can be blanched, usually smaller than 1 cm
  - Acral areas, especially subungual areas of fingers and toes
  - Hildreth sign-disappearance of pain after application of a tourniquet proximally on the arm
  - Love test-eliciting pain by applying pressure to a precise area with the tip of a pencil

- **Multiple variant (3 types)**
  - Regional variant-blue to purple compressible papules or nodules that are grouped and limited usually to an extremity
  - Disseminated type-less common variant with multiple lesions distributed over the body with no specific grouping
  - Congenital plaquelike glomus-rarest variant with tumors are either grouped papules that coalesce into indurated plaques or clusters of discrete nodules
Glomus Tumors

- **Solitary glomus tumors usually have paroxysmal pain**
  - Exacerbated by pressure or temperature changes, especially cold
  - Modified smooth muscle cells

- **Multiple glomus tumors can also be painful**
  - Less common
  - Pain usually is not severe
  - Autosomal-dominant condition - check for family history
Glomus Tumors

- Solid well-circumscribed nodules surrounded by a rim of fibrous tissue
- Endothelium-lined vascular spaces surrounded by clusters of glomus cells
- Glomus cells monomorphous round or polygonal cells with plump nuclei and scant eosinophilic cytoplasm
- Multiple lesions are less well circumscribed and less solid-appearing than their solitary counterparts.

Variants
- Glomangiomas
- Glomangiosarcomas—more atypia, pleomorphism, mitotic figures, and invasive growth pattern

Treatment
- Surgical excision
Glomus Tumors

- Study of 52 unusual glomus tumors previously diagnosed as "atypical" or "malignant" by virtue of nuclear atypia, infiltrative growth, or mitotic activity.
- **Malignant glomus tumor**
  - Deep location
  - Size of more than 2 cm, or
  - Atypical mitotic figures, or
  - Moderate to high nuclear grade and 5 mitotic figures/50 HPF
- **Sympathetic glomus tumor**
  - Tumors with high nuclear grade in the absence of any other malignant feature
- **Glomus tumor of uncertain malignant potential**
  - Tumors that lack criteria for malignant glomus tumor or sympathetic glomus tumor but have high mitotic activity and superficial location only, or large size only, or deep location only
- **Glomangiomatosis**
  - Tumors with histologic features of diffuse angiomatosis and excess glomus cells.
- Conclusions
  Using this classification scheme, metastasis was observed in 38% of tumors fulfilling the criteria for malignancy. In contrast, metastatic disease was not seen in any specimen classified as sympathetic glomus tumor, glomus tumor of uncertain malignant potential, or glomangiomatosis.

Painful Dermal Tumors

- Angiolipoma
- Neuroma
- Glomus Tumor
- Eccrine spiradenoma
- Leiomyoma
Painful Dermal Tumors

- Blue rubber bleb nevus
- Leiomyoma
- Eccrine poroma/eccrine spiradenoma
- Neuroma
- Dermatofibroma/Dercum's disease (adiposis dolorosa)
- Angiolipoma
- Neurilemoma
- Endometrioma
- Glomus tumor
- Granular cell tumor
Dabska Tumor

- Dabska described in 1969 as malignant endovascular papillary angioendothelioma
- Slow-growing, painless, intradermal nodule up to 2-3 centimeters in diameter
  - May grow to 40 cm in diameter
  - Occasionally satellite nodules
- Violaceous, pink, or bluish-black in coloration
- Head and extremities most common
Dabska Tumor

- Normal overlying epidermis
- Dermis has multiple vascular channels that interconnect lined by atypical endothelial cells
  - Papillary structure lined with atypical columnar endothelial cells with central hyalinized core and project into a lumen lined by atypical columnar endothelial cells
  - Endothelial cells are cuboidal to tall cylindrical with vacuolated cytoplasm and hyperchromatic eccentric nuclei on their luminal border
  - Mitotic figures uncommon
  - Many intraluminal lymphocytes may be evident, often attached to the endothelial cells
  - Focal changes characteristic of retiform hemangioendothelioma occasionally may be observed
- IPOX
  - Intravascular proliferations may stain actin-positive.
- Ultrastructure
  - Irregular nuclei, abundant perinuclear cytoplasmic filaments, and many pinocytotic vesicles. Weibel-Palade bodies may be evident
  - Hyaline globules consist of electron-dense basement membrane material
Dabska Tumor

- Intermediate grade angiosarcoma
  - Three of the original 6 cases locally aggressive, with tumor invasion into bone, musculature, fascia, and/or tendons
  - One of Dabska's original 6 cases died of widespread pulmonary metastases
- Wide local excision
- Recurrence unusual
- Regional lymph node dissection considered, especially if palpable lymph nodes
Questions

- Man is certainly stark mad; he cannot make a flea, yet he makes gods by the dozens.

Michel de Montaigne (1533 - 1592)