Vascular Tumors- In Medusa's Image

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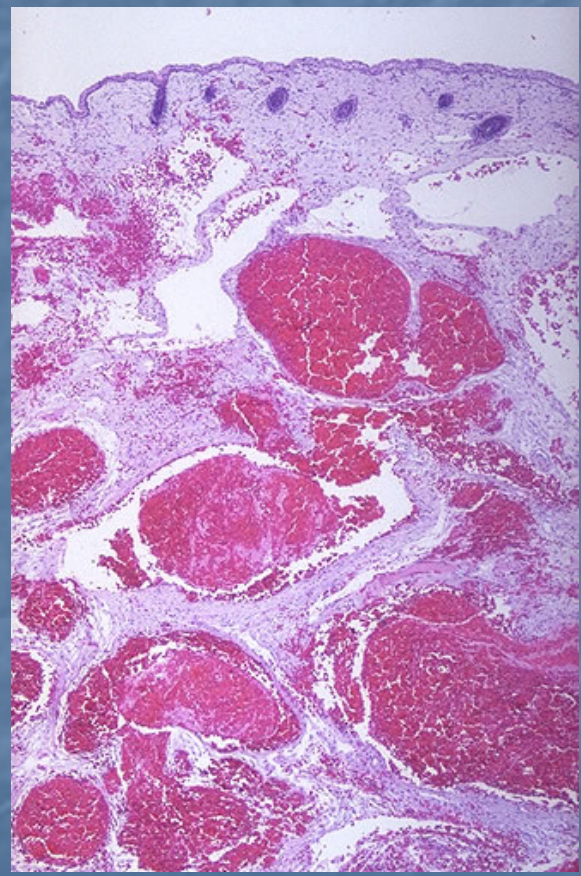
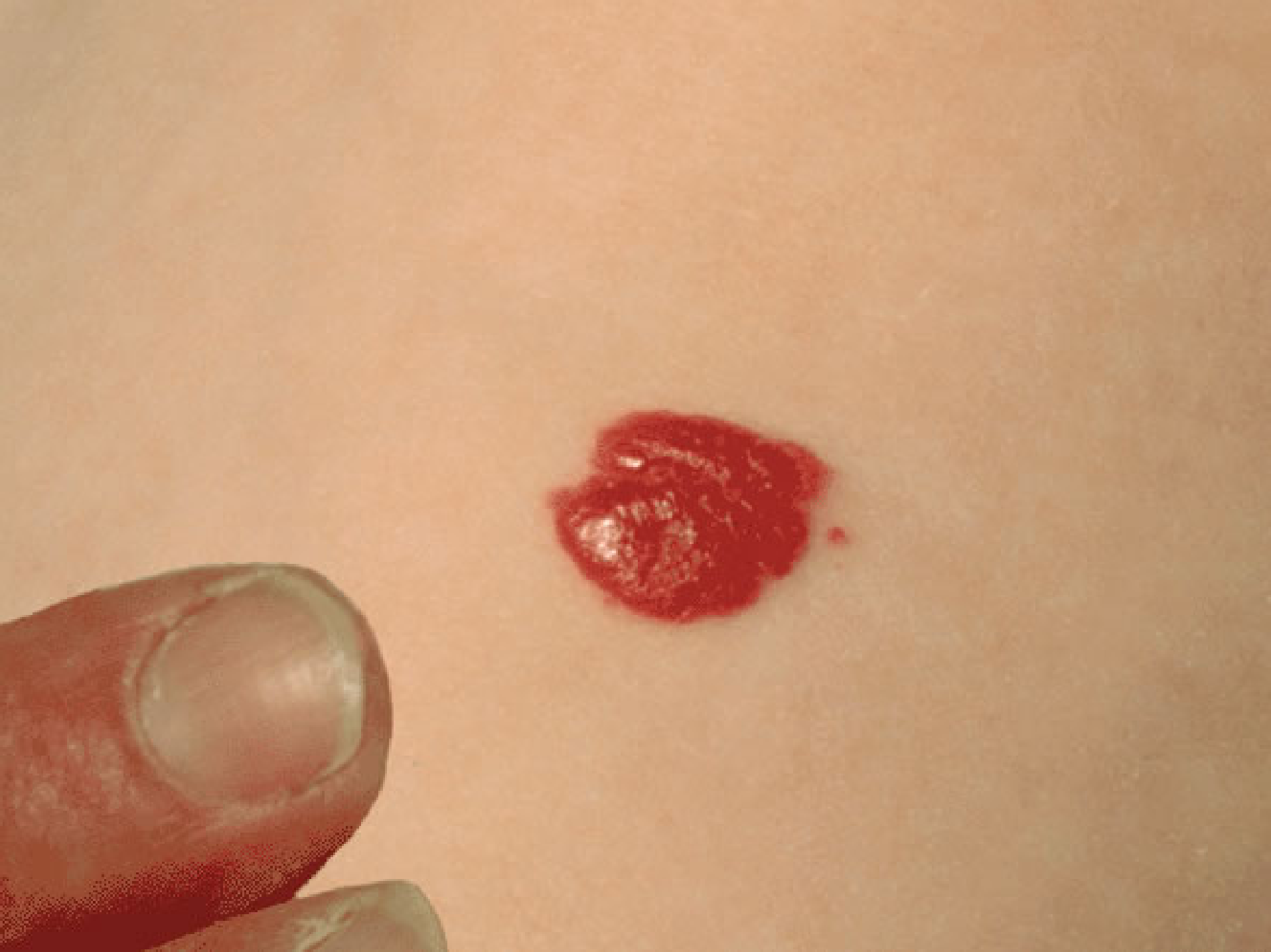
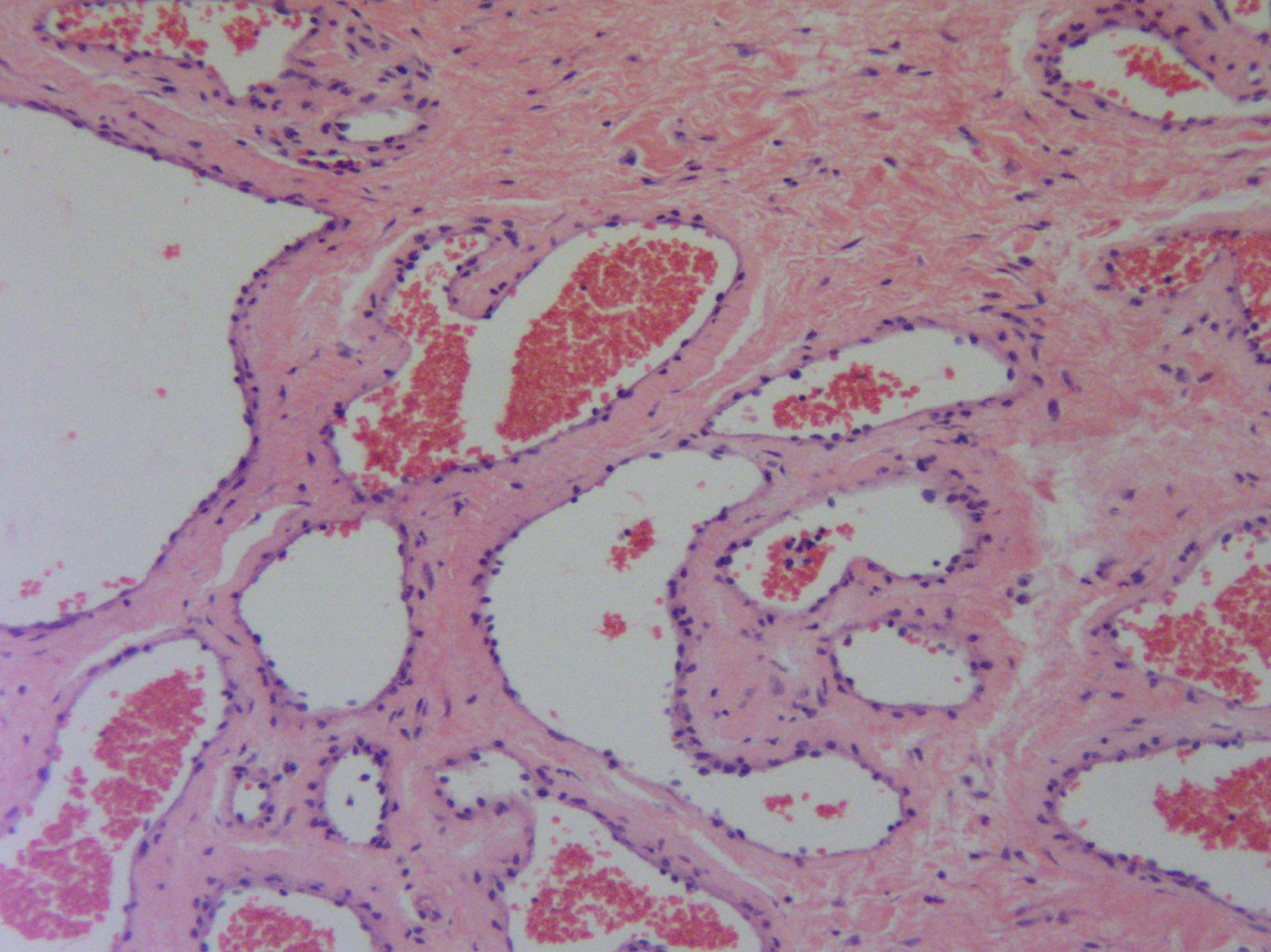
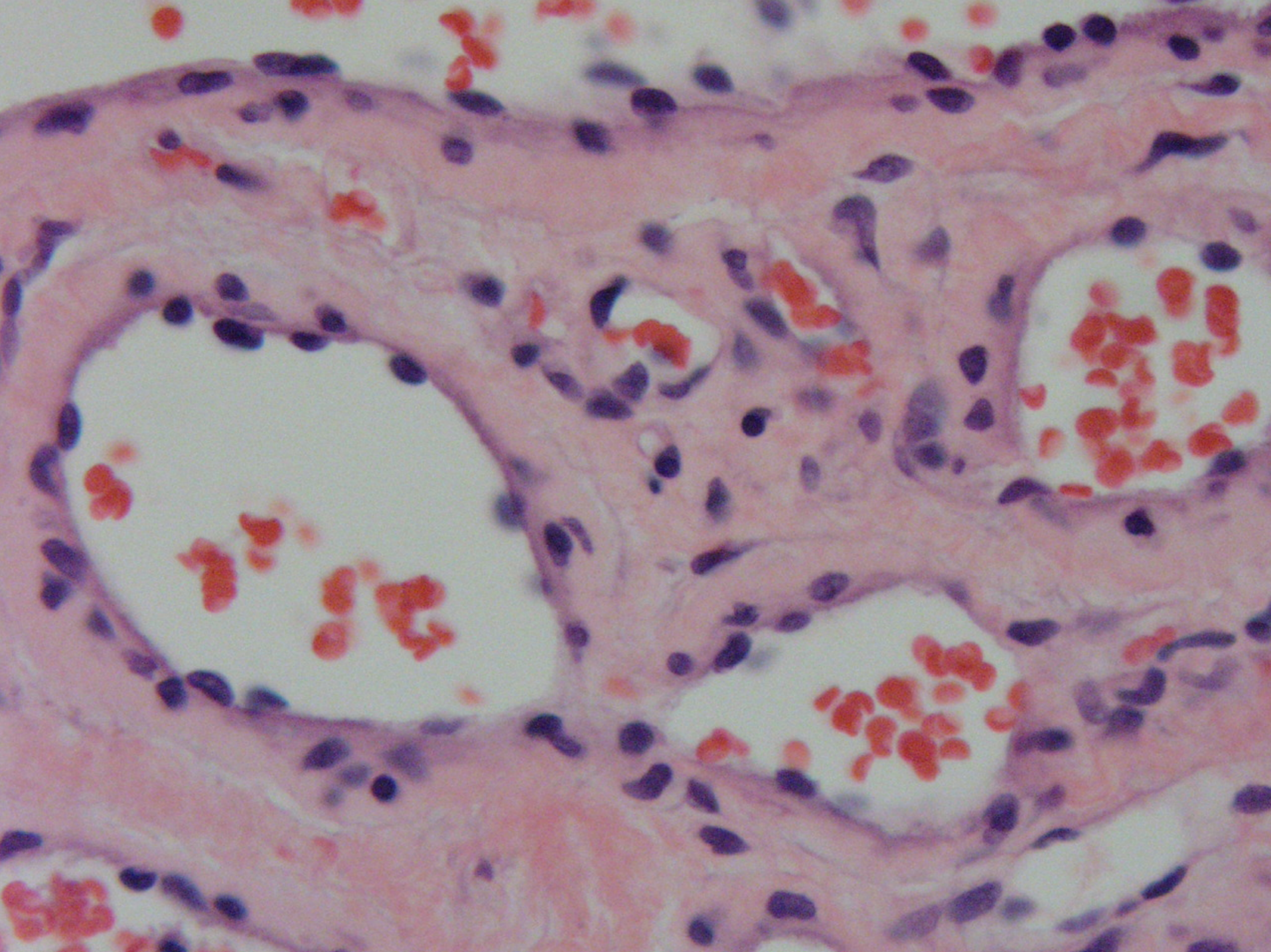
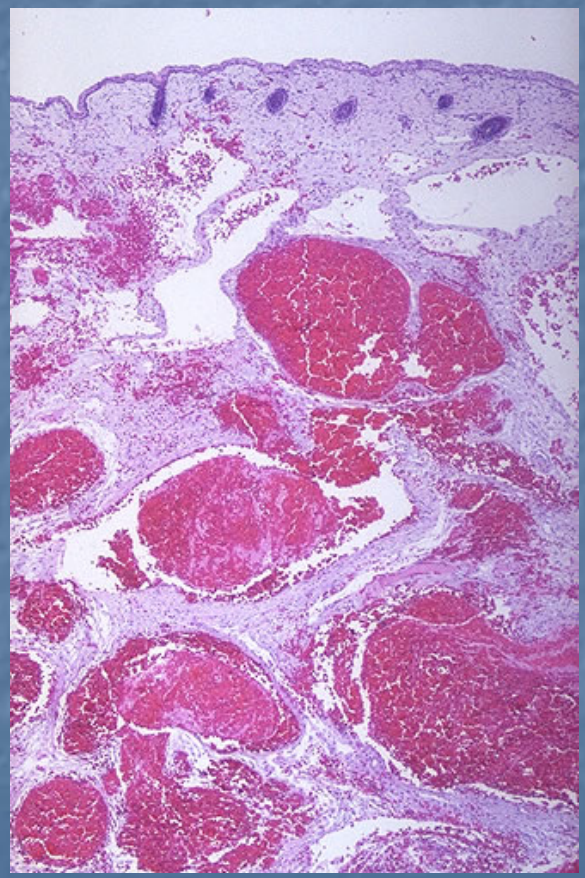








Capillary Hemangioma



- 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

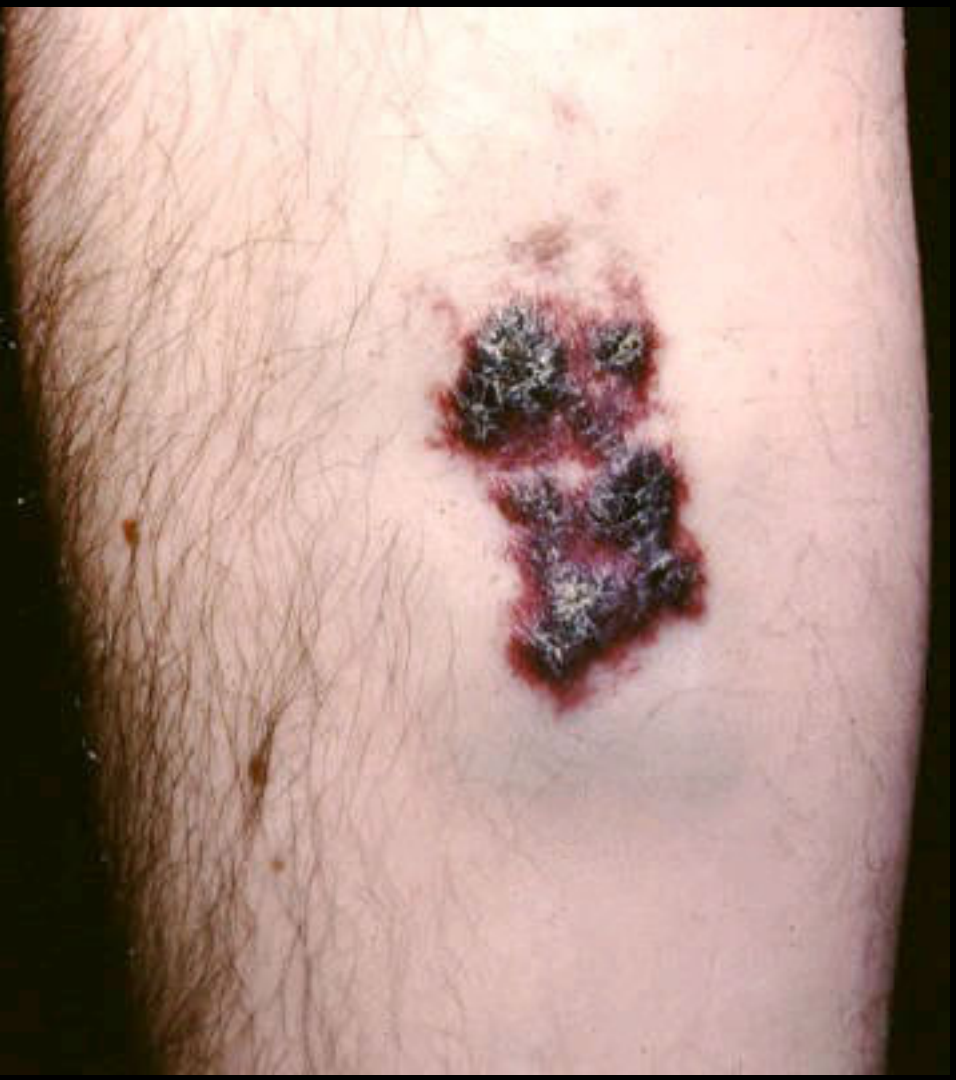
- Kasabach-Merritt syndrome
  - Mortality rates from 30-50%
  - Consumption coagulopathy and thrombocytopenia secondary to platelet sequestration
  - Disseminated intravascular coagulation
  - High-output congestive heart failure
- Ophthalmic morbidity
  - Space-occupying effects
  - Deprivation amblyopia in the affected eye if the lesion is large enough to directly occlude the visual axis
  - Anisometropic amblyopia if corneal distortion and astigmatism occur

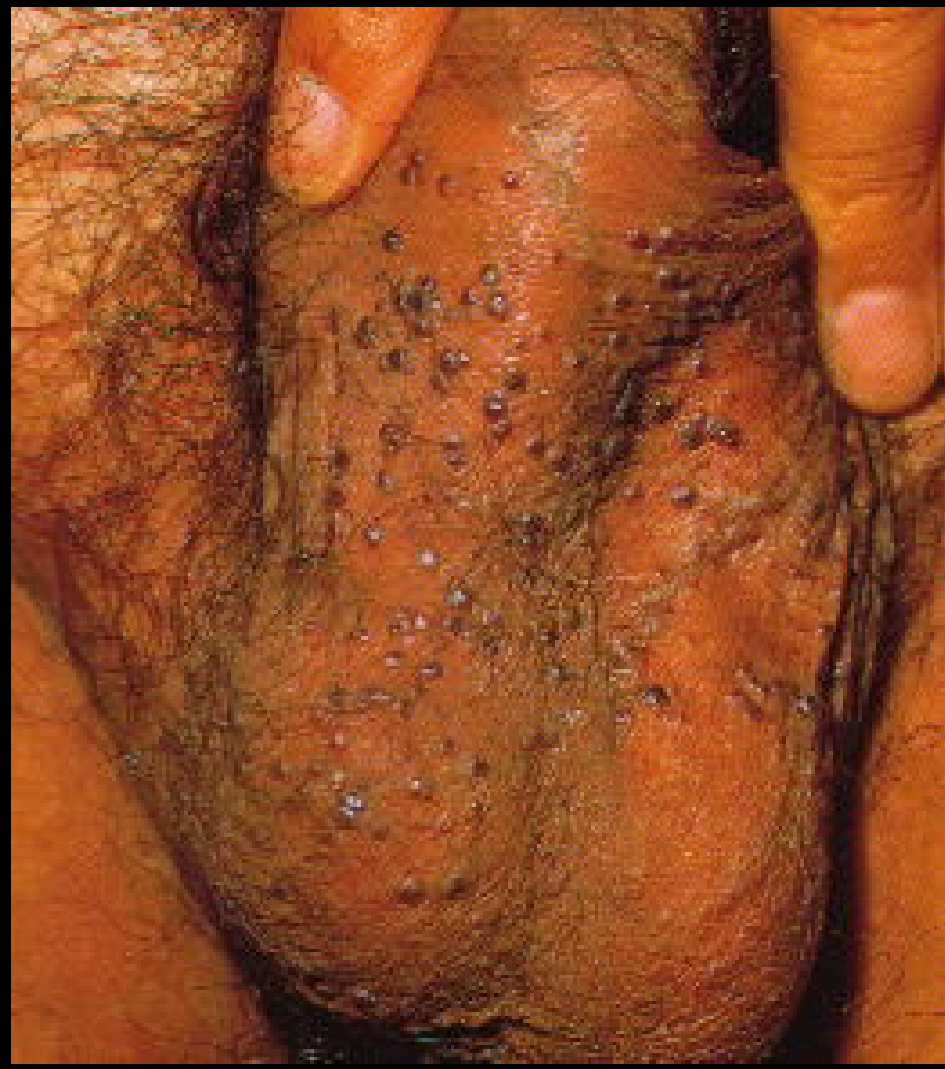
Treatment

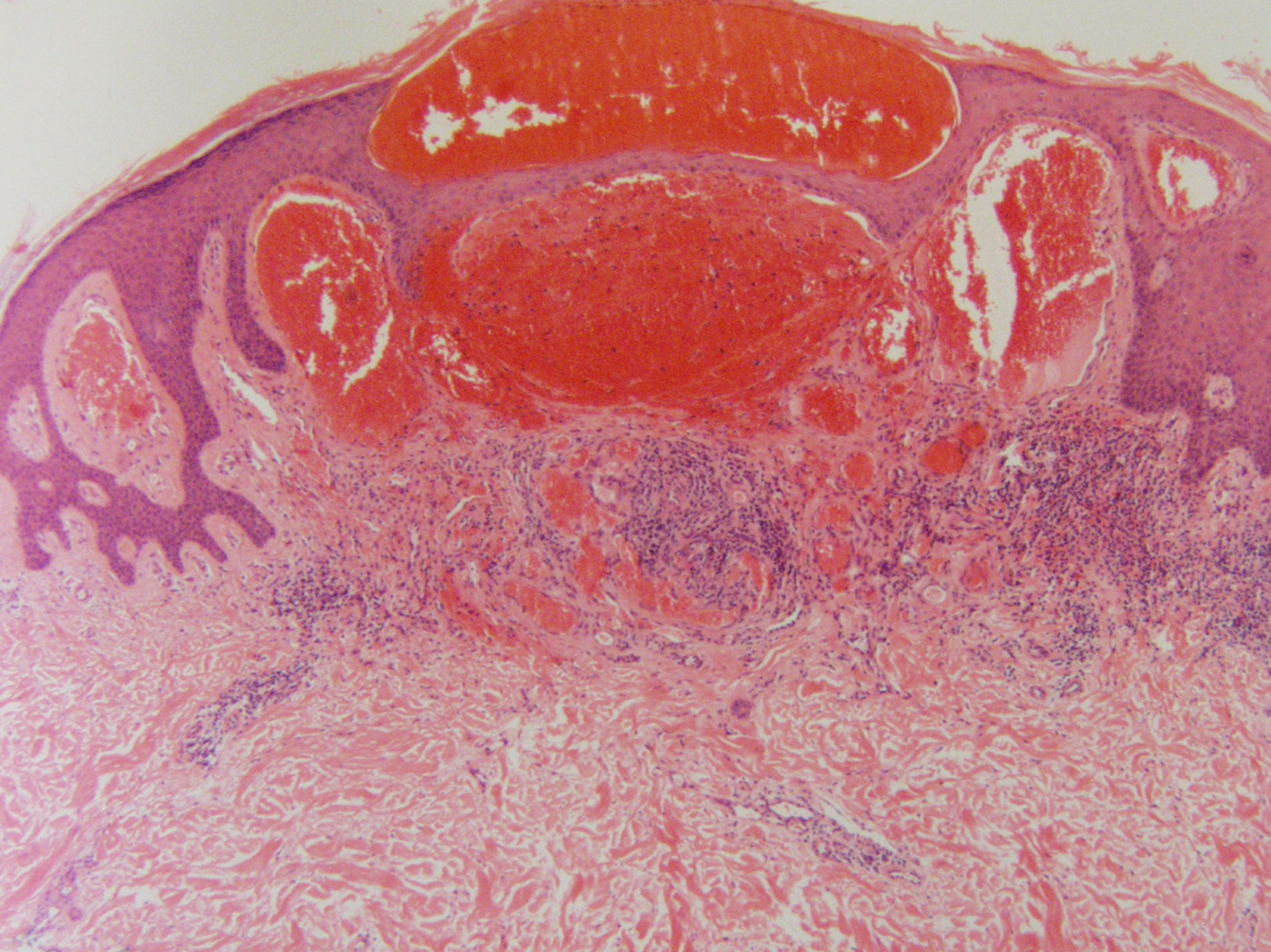
- Observation!
- Corticosteroids
  - Topical steroid formulations for cutaneous lesions
  - Injectable steroid formulations also are used in the treatment of these lesions.
  - Systemic corticosteroids are used for amblyogenic life-threatening lesions.
    - Excellent response in 30% of patients, a questionable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

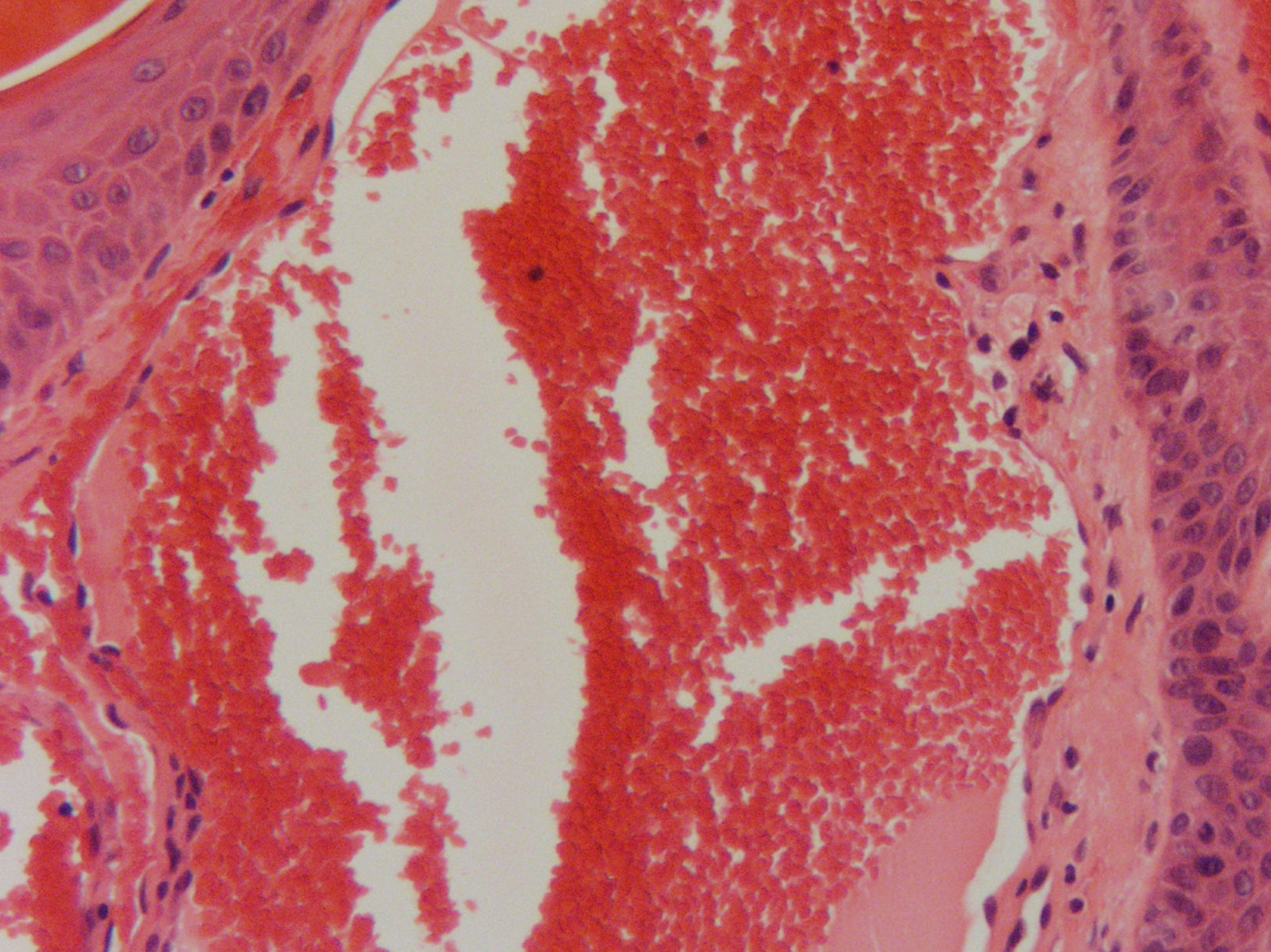
Treatment

- 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









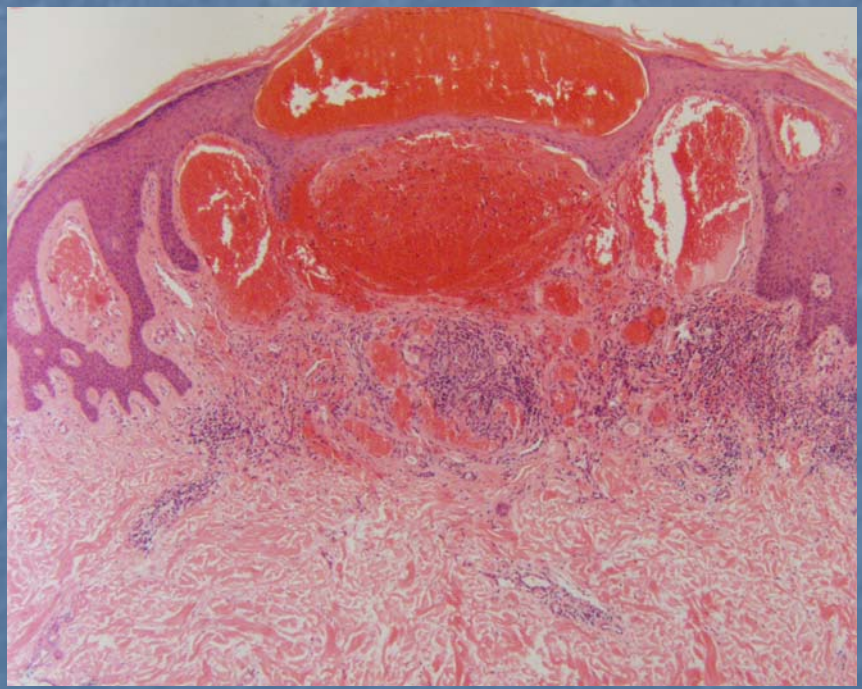
Angiokeratoma

- 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

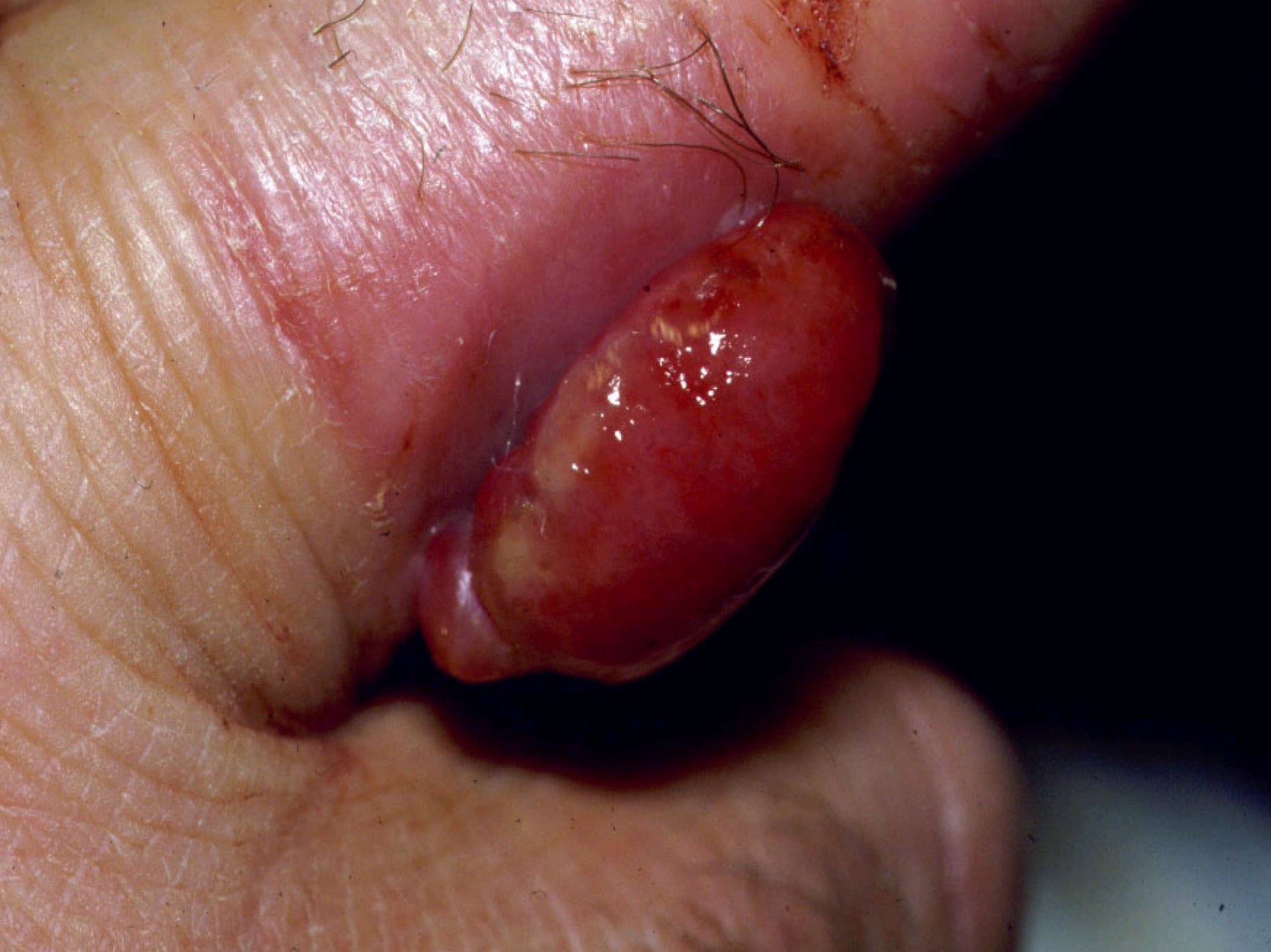
Angiokeratoma

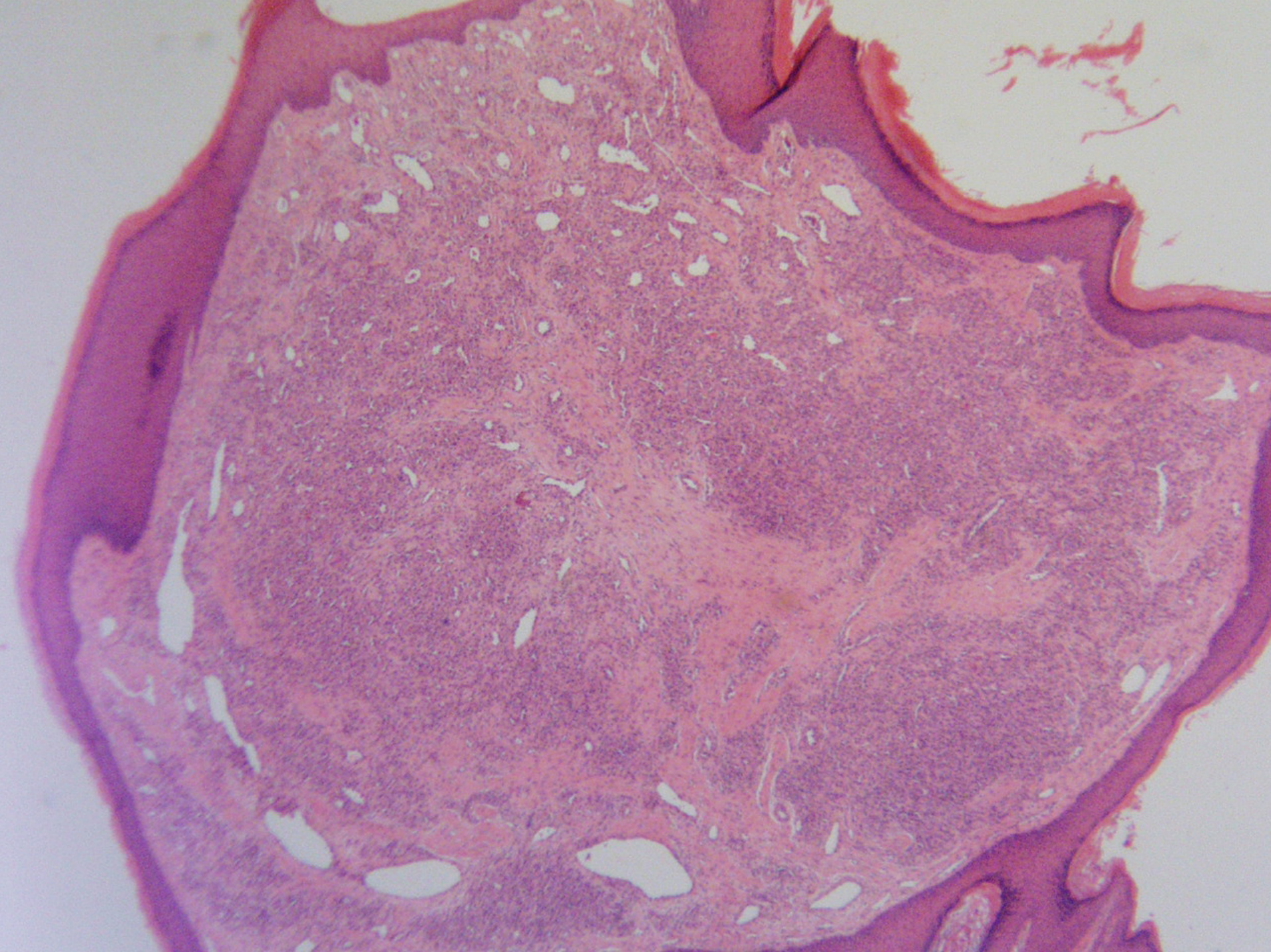
- Clinical variants
  - Angiokeratoma circumscriptum (Angiokeratoma corporis neviform)
  - Angiokeratoma Mibelli-type on the fingers and the toes
  - Fabry's disease (on a lower extremity or the trunk)
  - Angiokeratoma of Fordyce (found on the scrotum)
  - Caviar spots (angiokeratomas of the tongue)
- Clinical associations
  - Cobb syndrome
    Klippel-Trenaunay syndrome
    Nevus flammeus
    Cavernous hemangiomas
    Traumatic arteriovenous fistulas

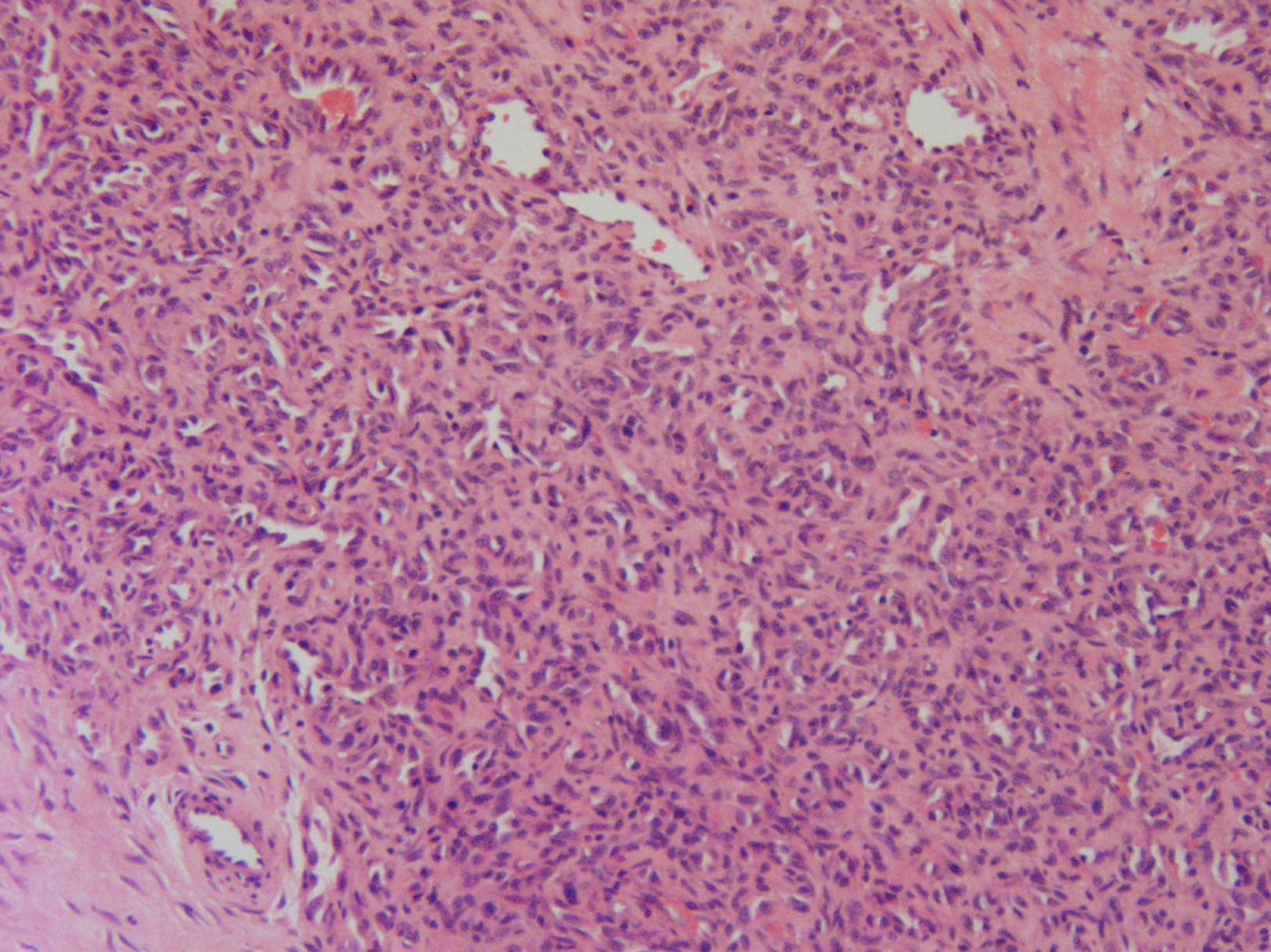
Angiokeratoma

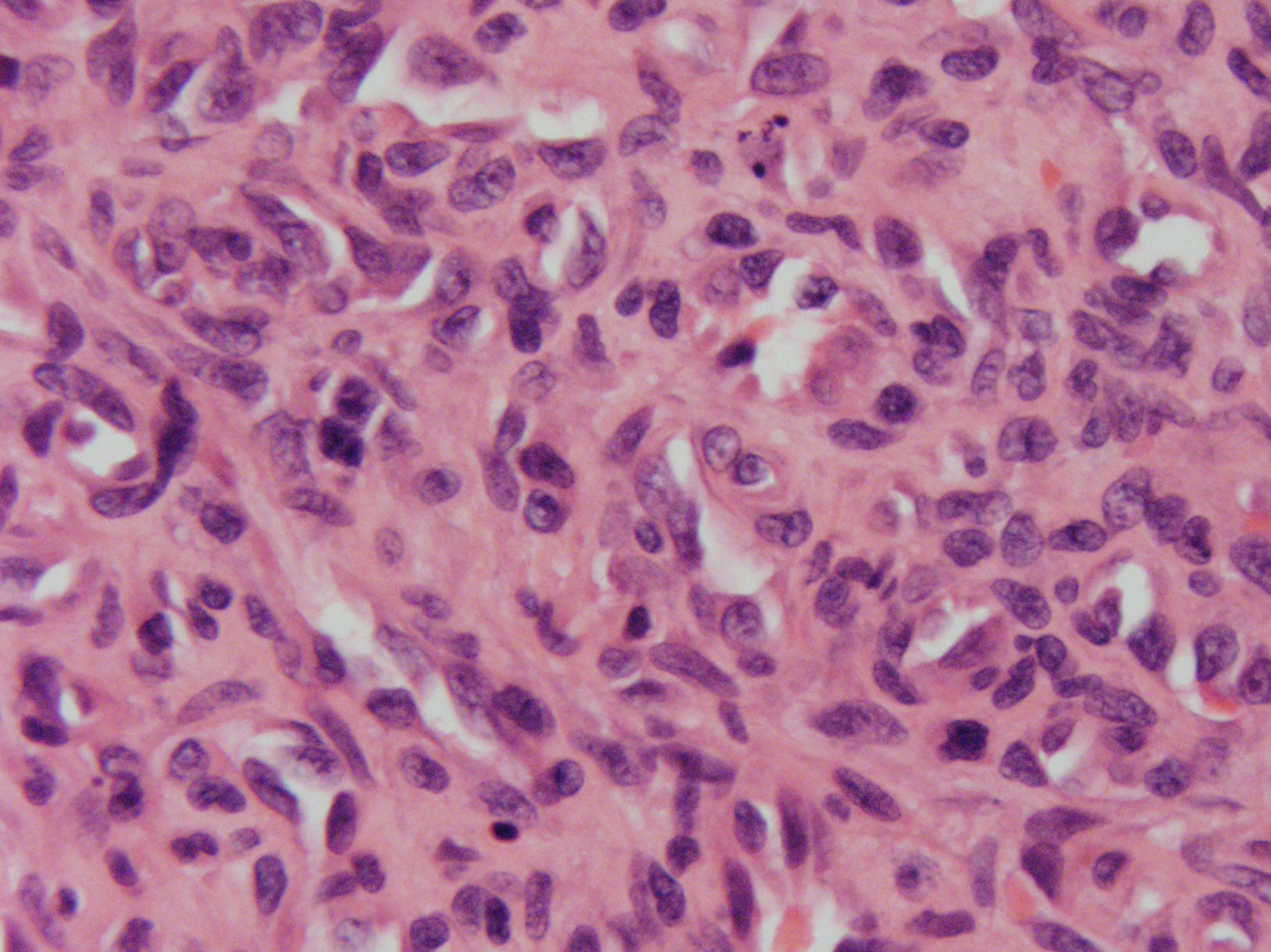


- Exophytic profile with numerous ectatic thin-walled vascular channels surrounded by epidermal collarette
- Thrombosis of these vessels is common
- Clinically may mimic melanoma
- Fabry disease-may contain cytoplasmic vacuoles in endothelial cells, fibroblasts, and pericytes
- Treatment
  - Usually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









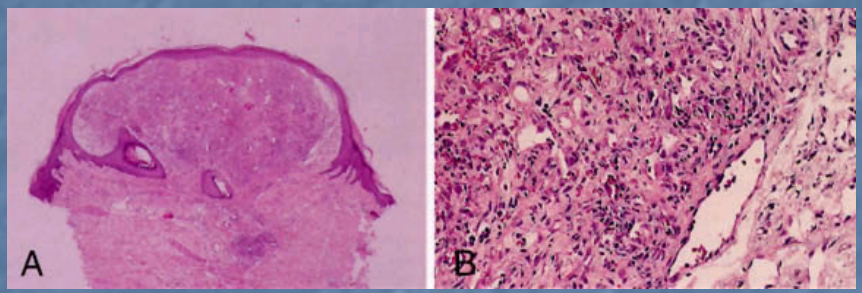
Pyogenic Granuloma (Lobular capillary hemangioma)

- 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

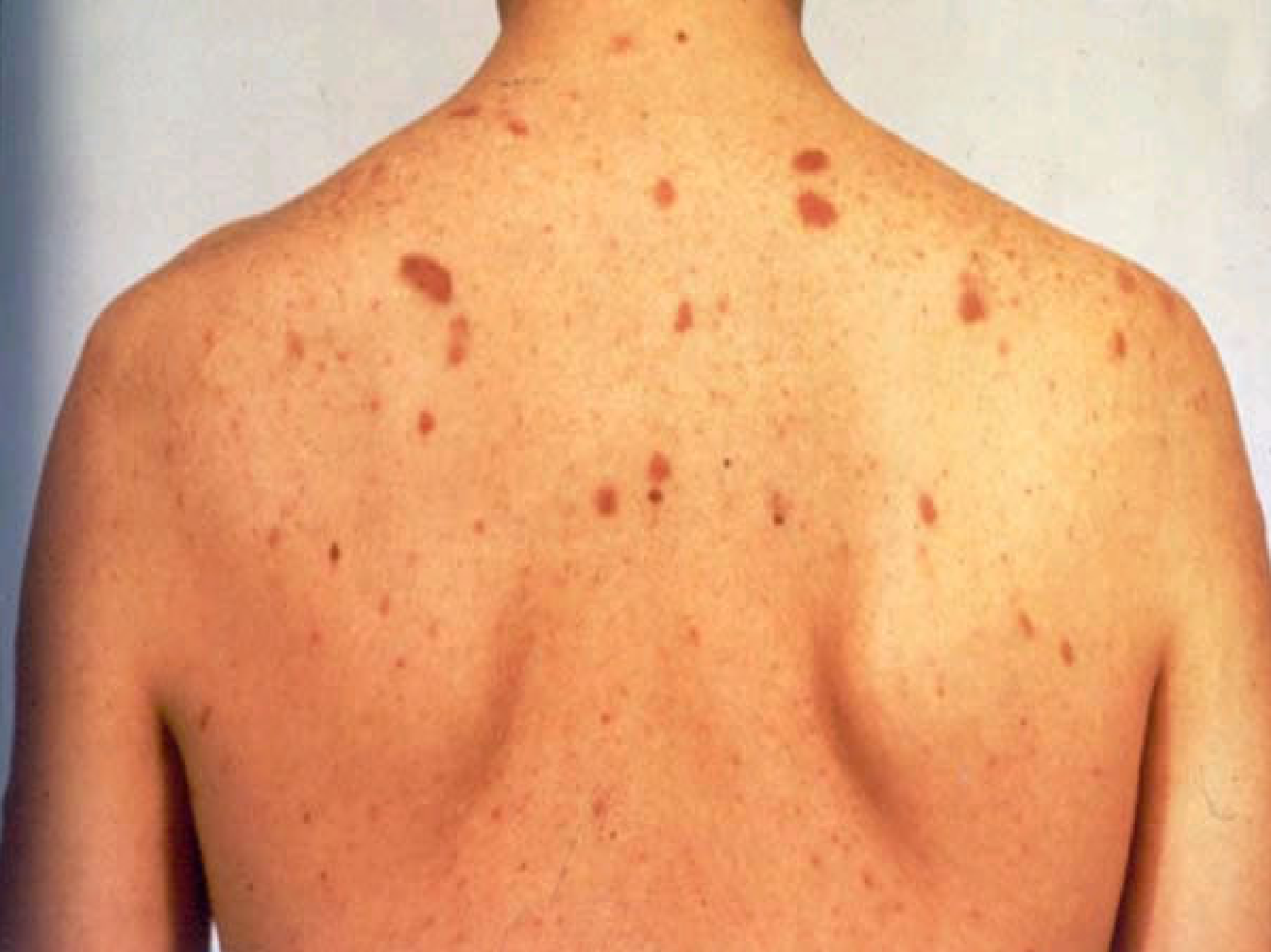
Pyogenic Granuloma

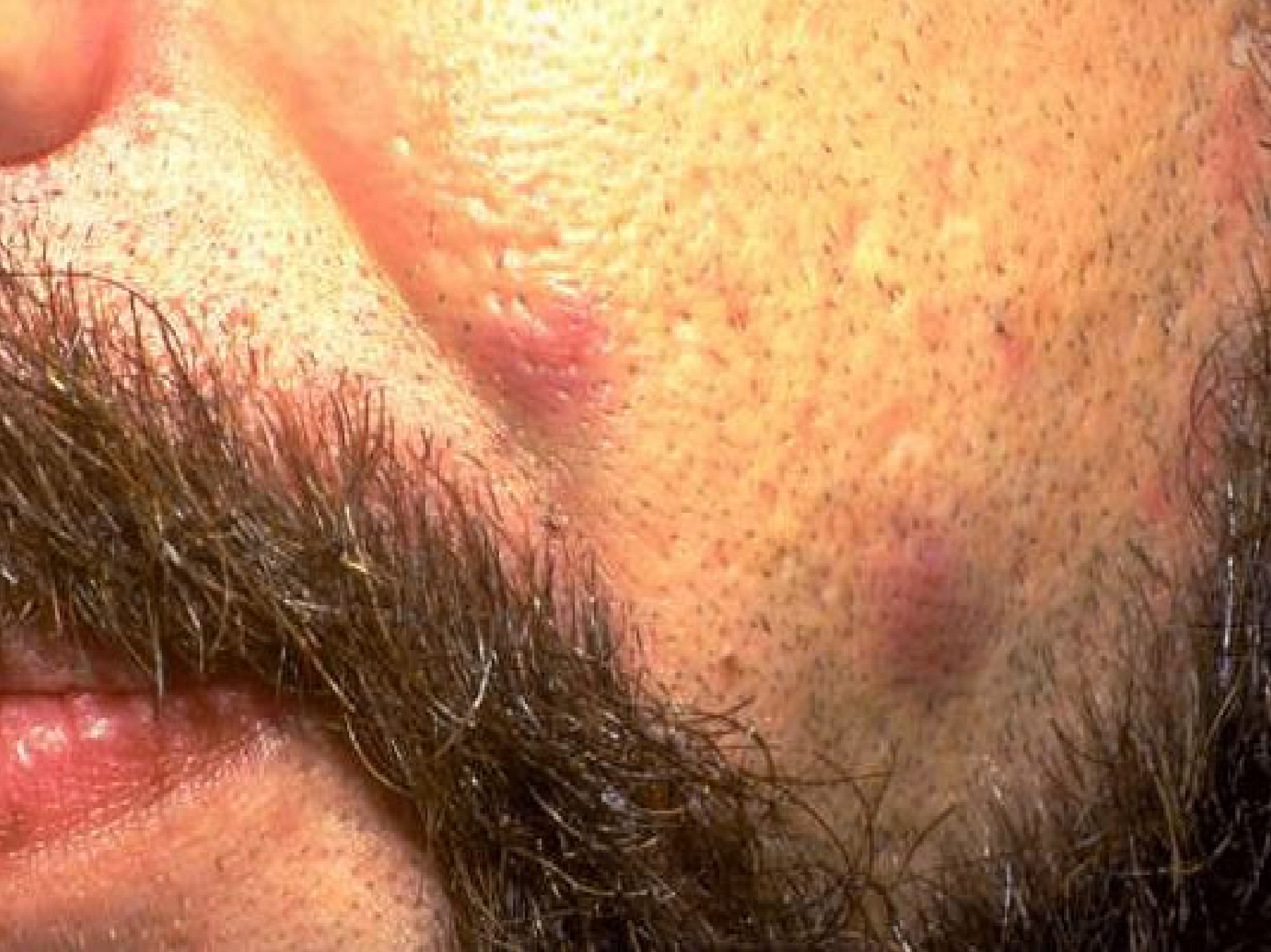
- Rapid growth, often with history of trauma
- Uncommon variants
  - PG with satellitosis
  - Intravenous PG
- Treatment
  - Removal by surgery or laser

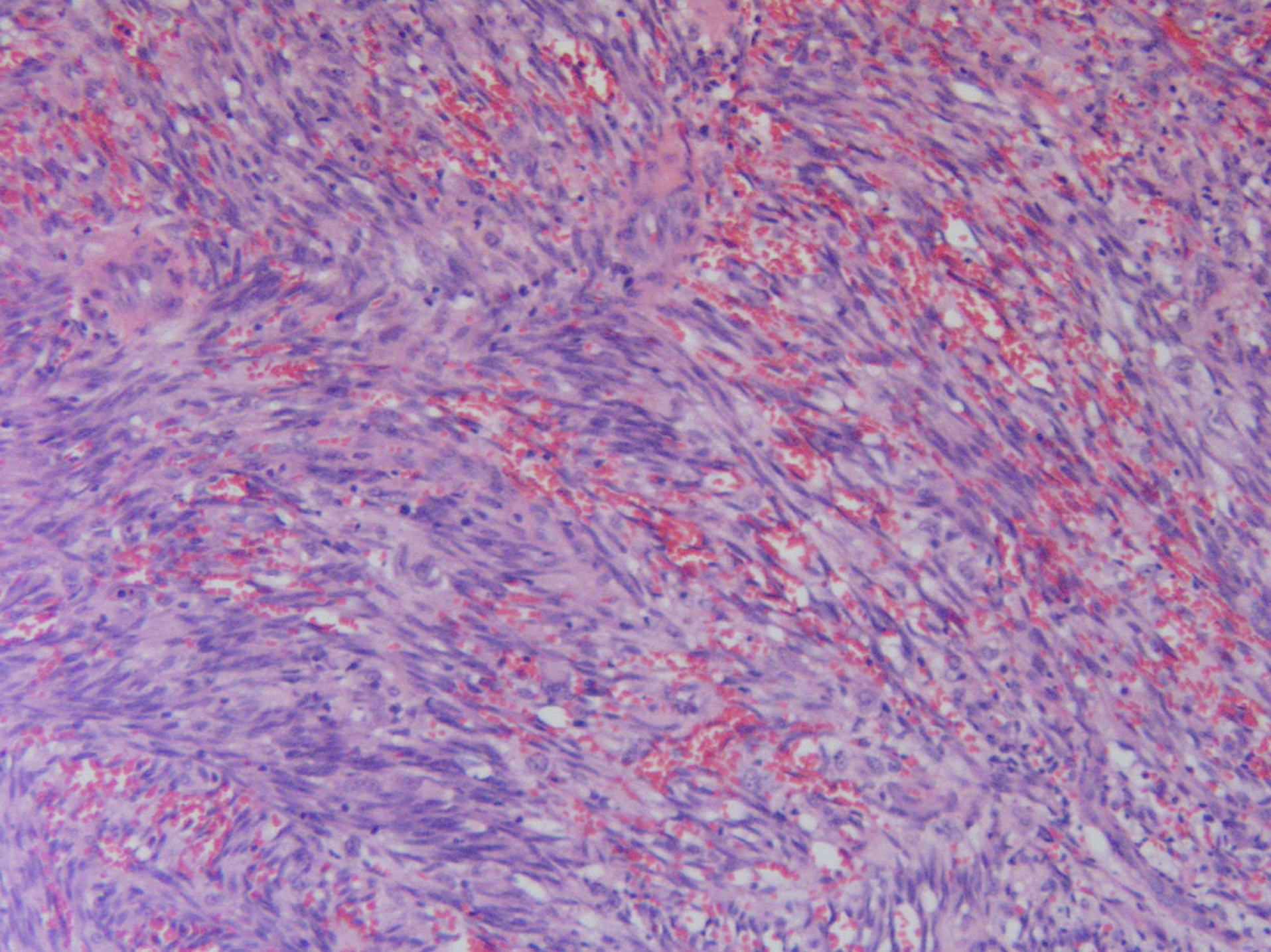
Pyogenic Granuloma DDX

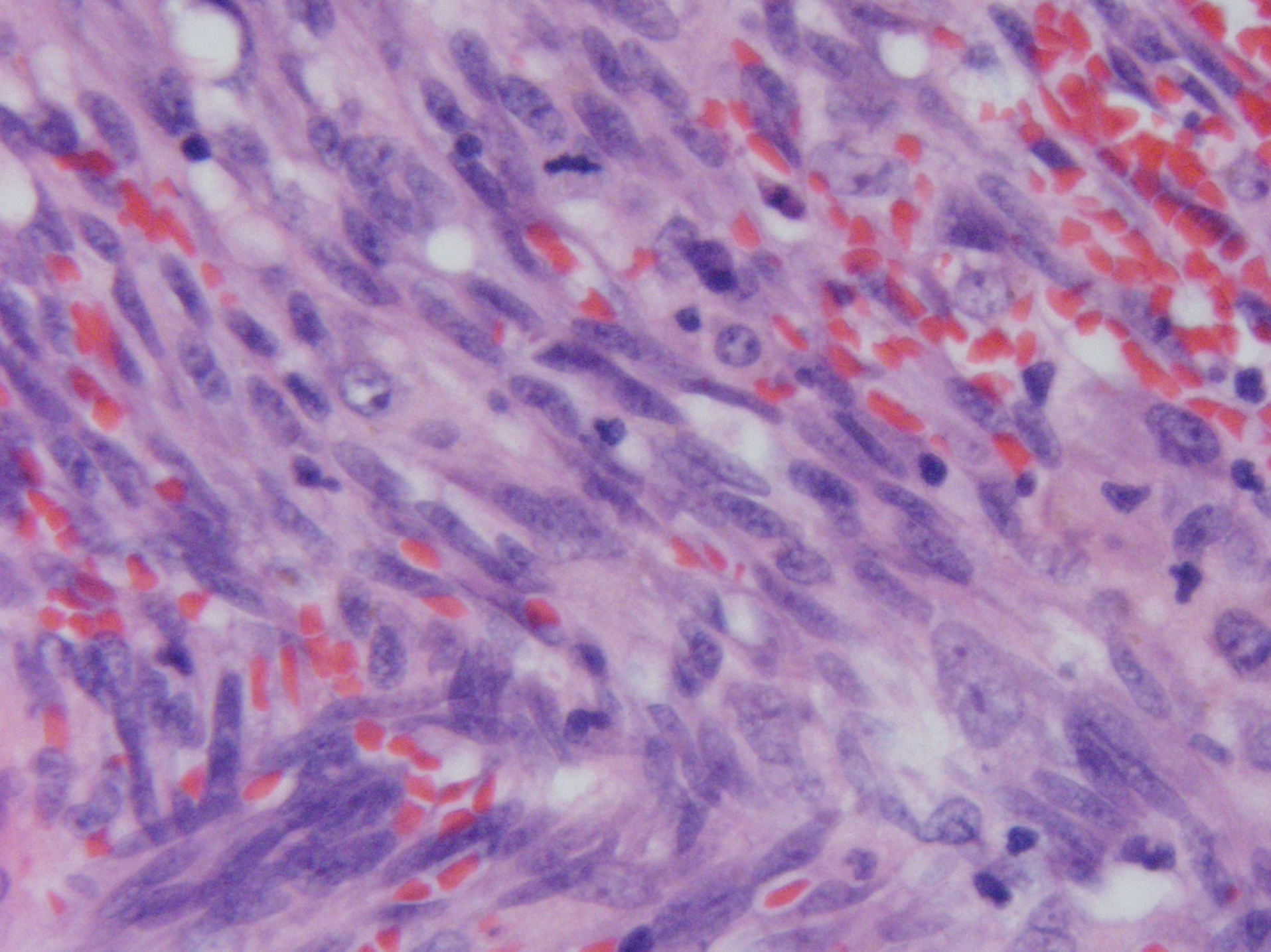


- Bacillary angiomatosis
  - Clinical history
  - Neutrophils adjacent to the blood vessels
  - Granular material resembling fibrin
  - Warthin-Starry silver or GMS stain









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

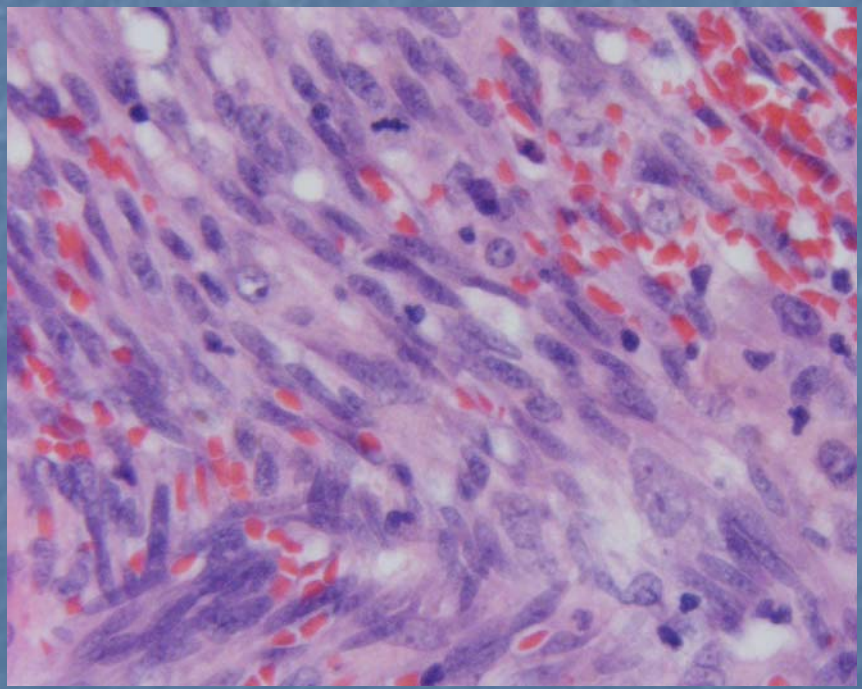
KS and HHV-8

- 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

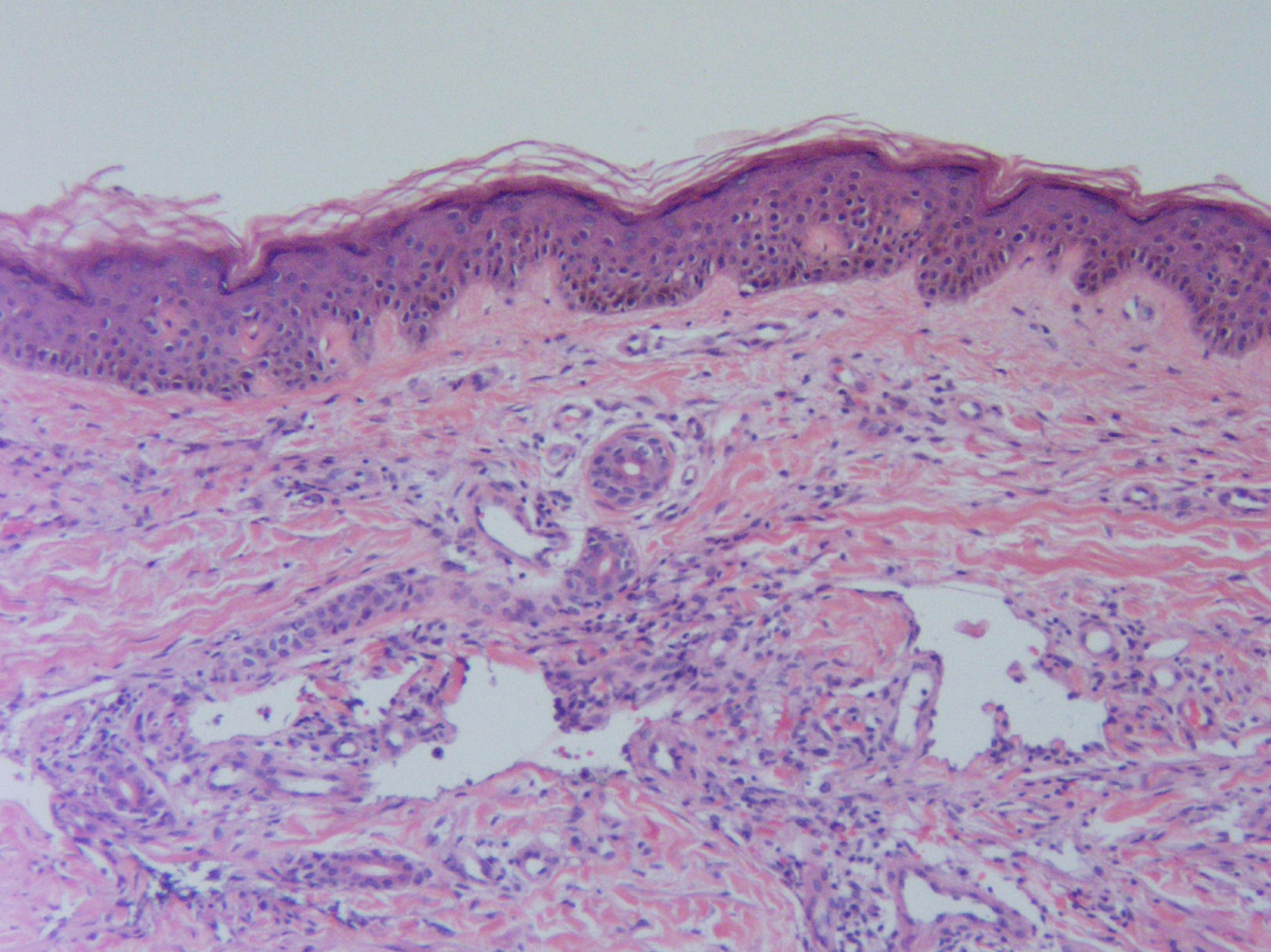
Kaposi Sarcoma

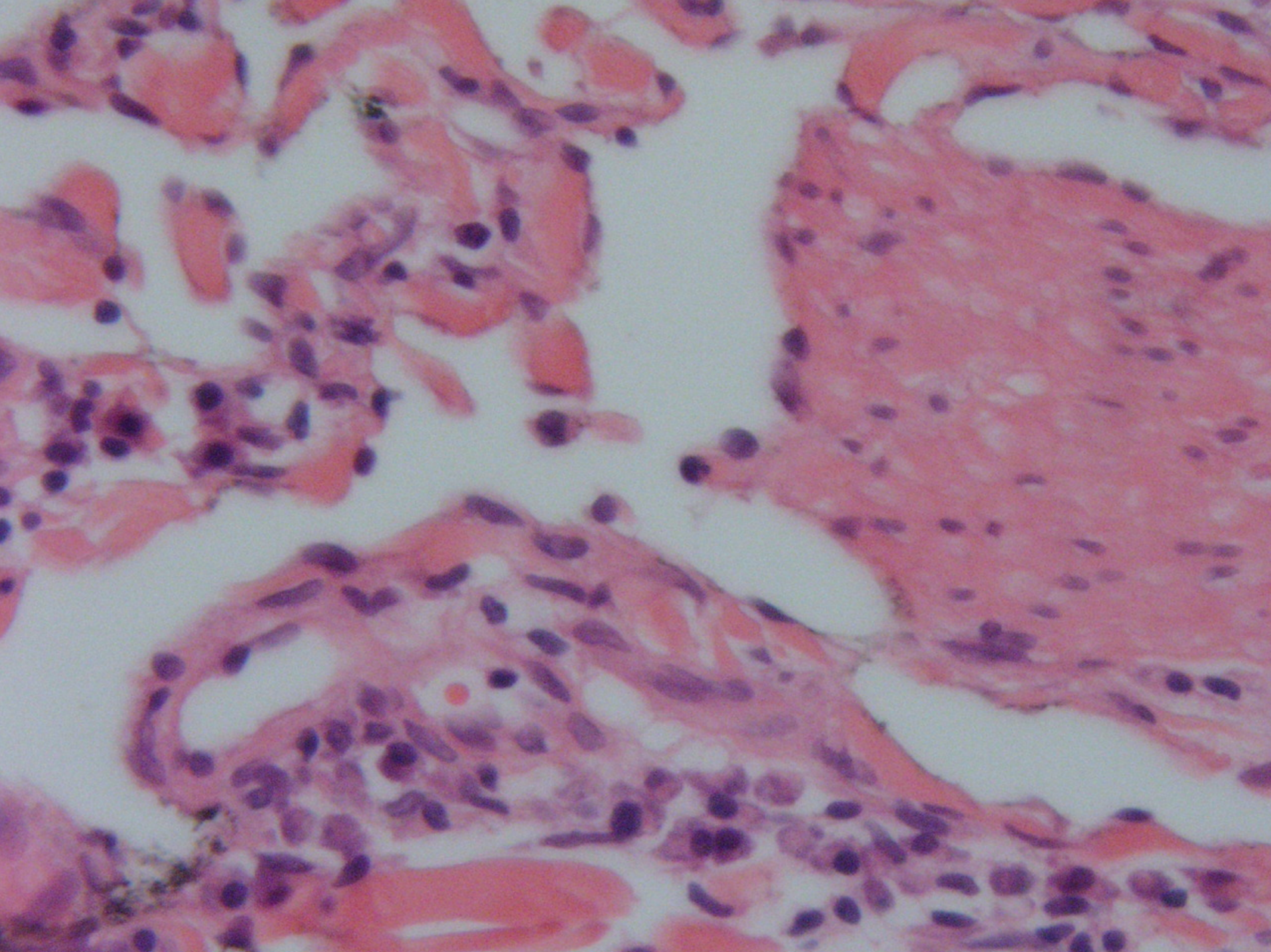
- Cutaneous lesions any location but usually lower extremities and the head and neck region
- Palpable and nonpruritic, macular, papular, nodular, or plaquelike appearances
- Several millimeters to several centimeters in diameter
- Brown, pink, red, or violaceous color and may be difficult to distinguish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

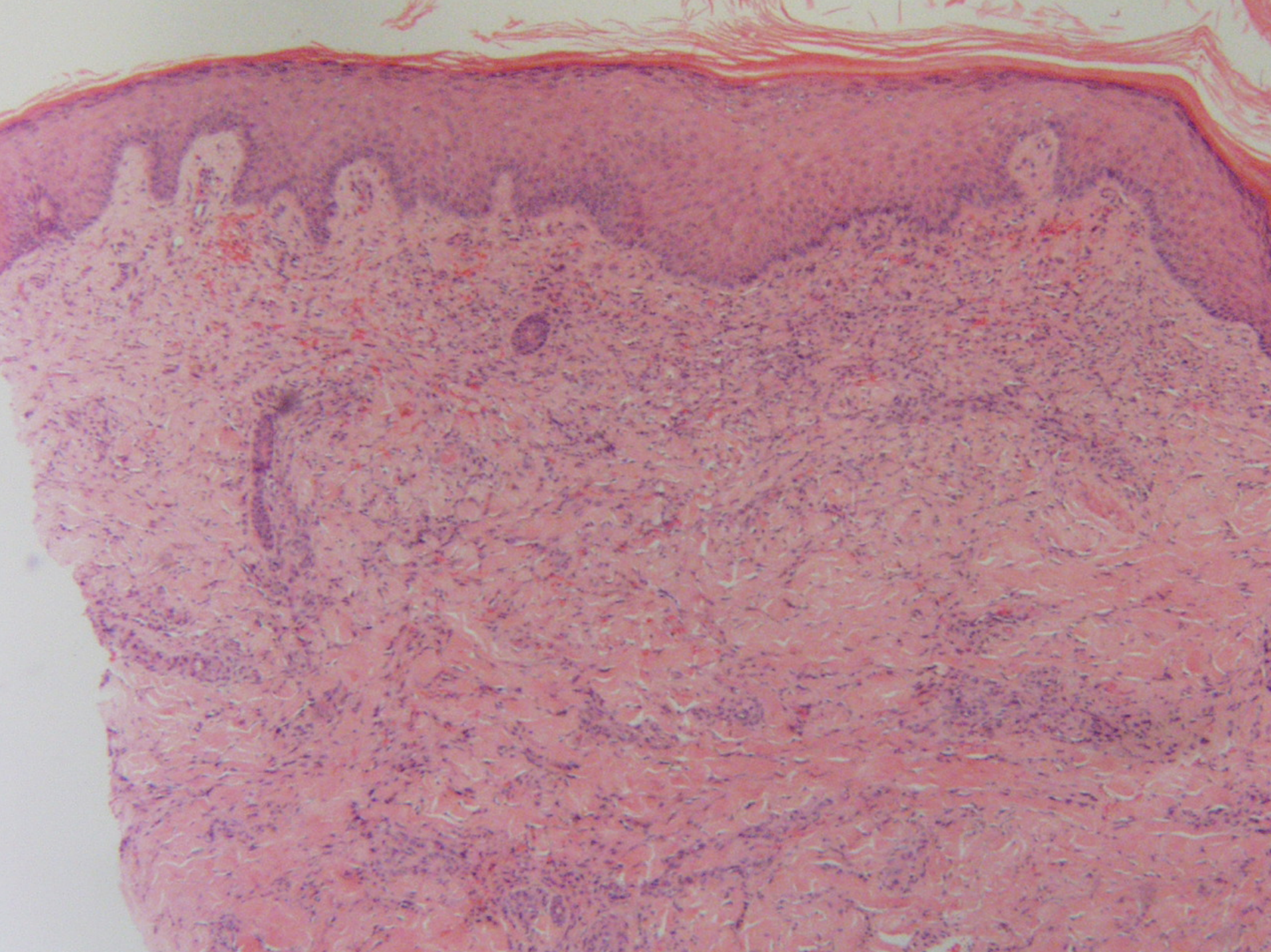
KS-Histopathology

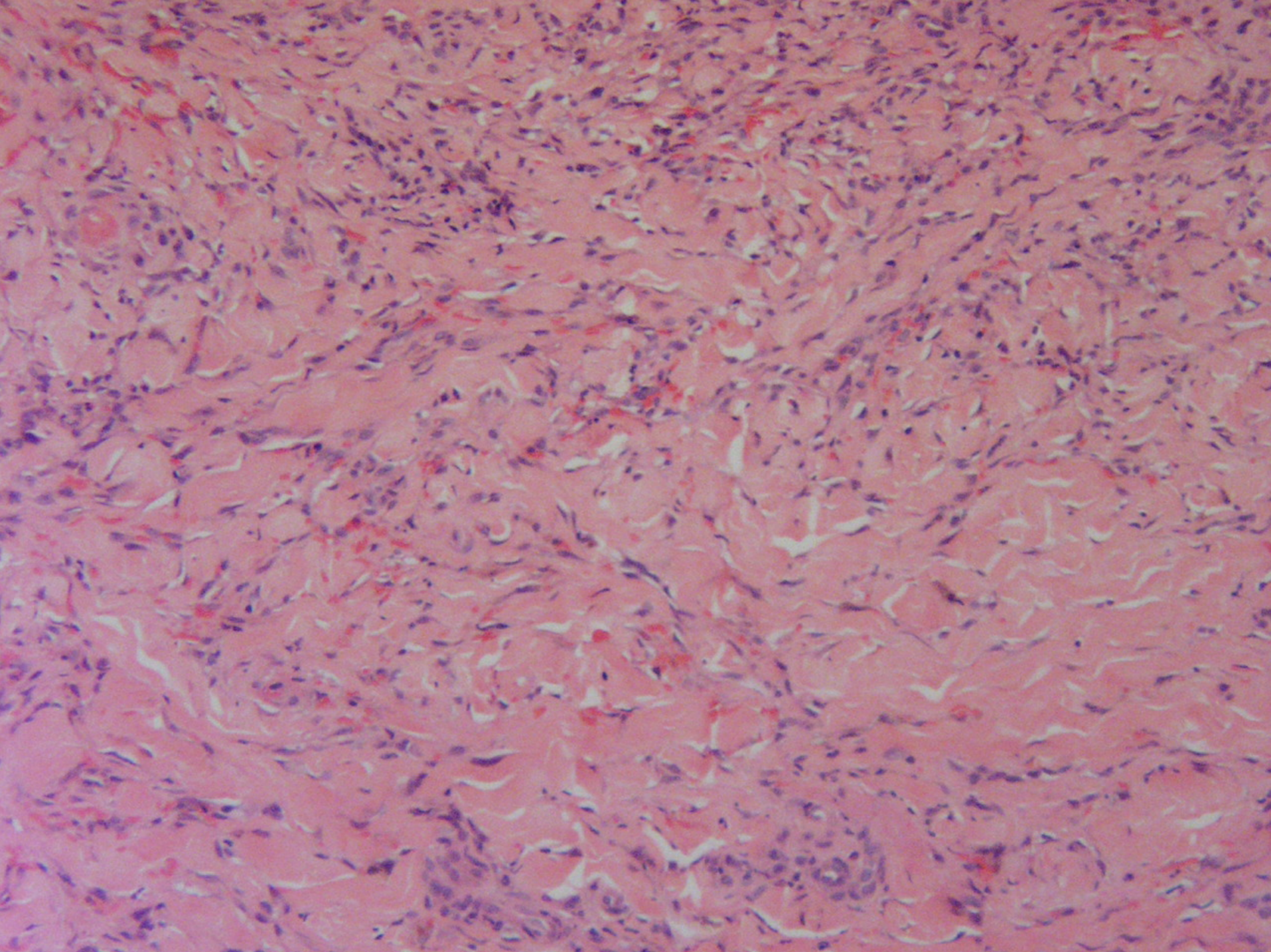


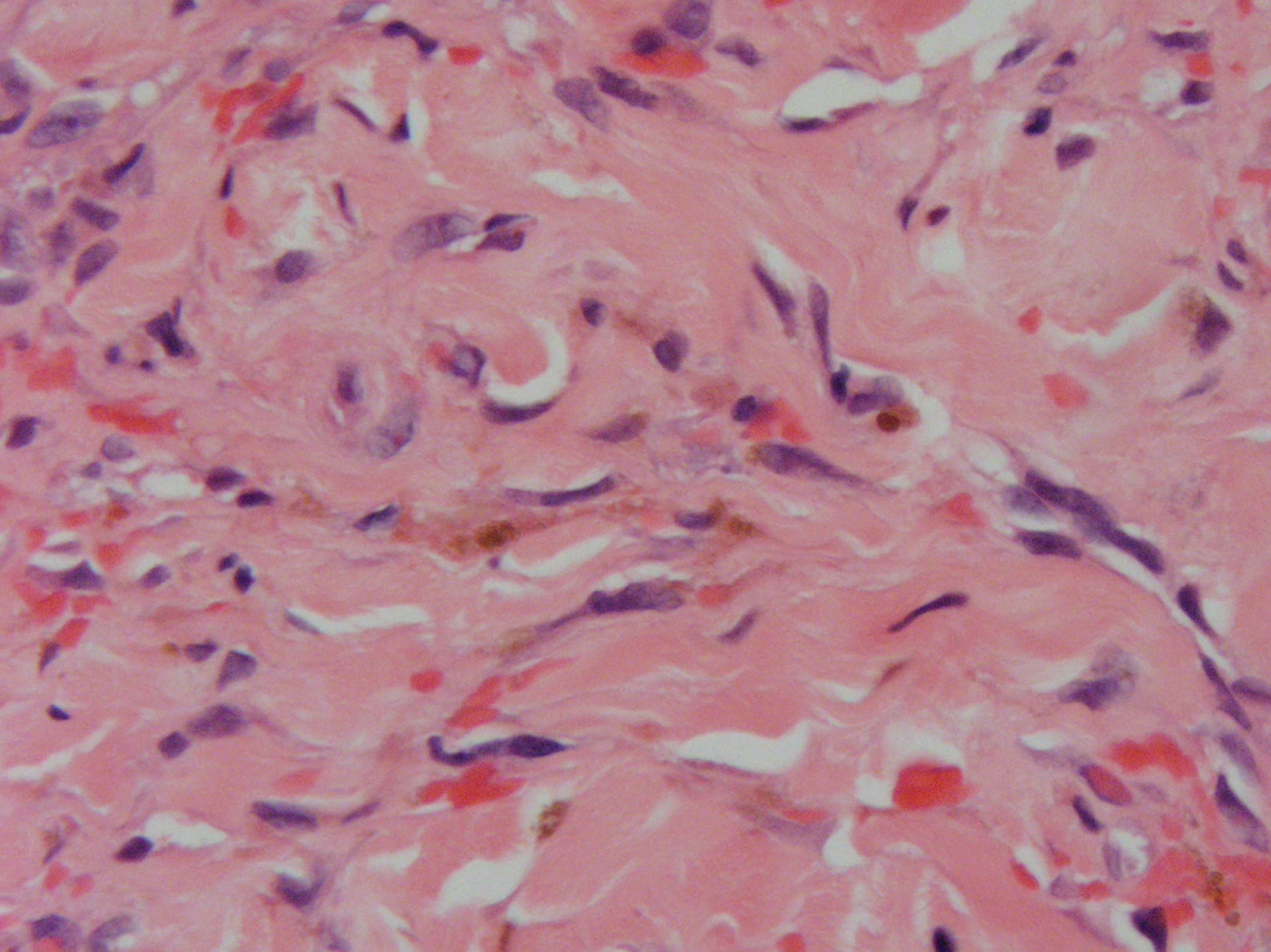
- Proliferation of spindle cells, prominent slitlike vascular spaces, and extravasated red blood cells
- Hyaline globules, PAS positive
- Promontory sign in early lesions











Kaposi Sarcoma

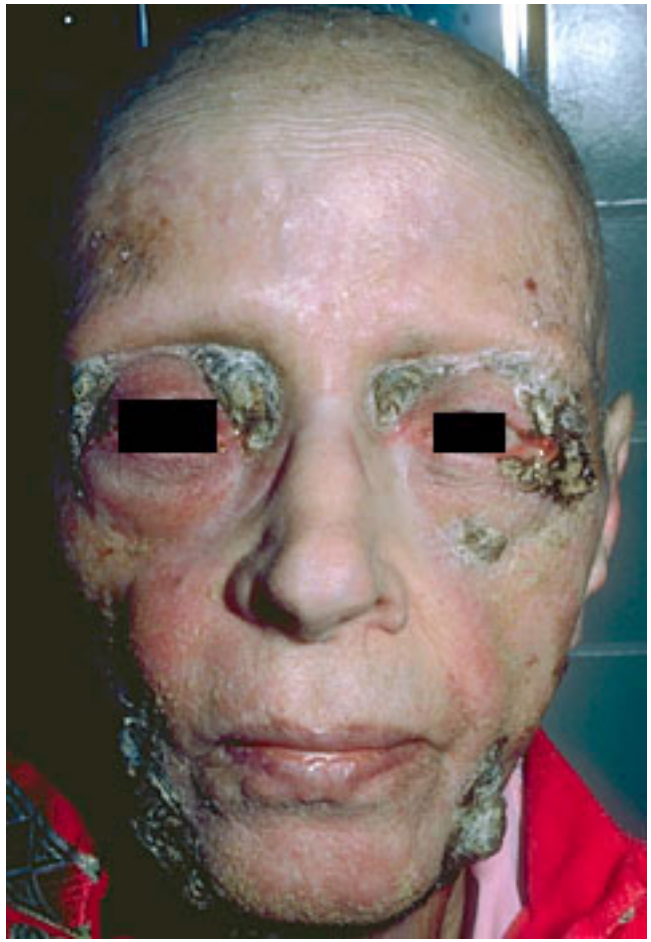
- AIDS Clinical Trials Group (ACTG) proposed staging system
- Good risk
  - Tumor (T) - Confined to skin and/or lymph nodes and/or minimal oral disease
  - Immune system (I) - CD4 greater than 200/mm3
  - Systemic illness (S) - No history of opportunistic infection, more than 10% involuntary weight loss, 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

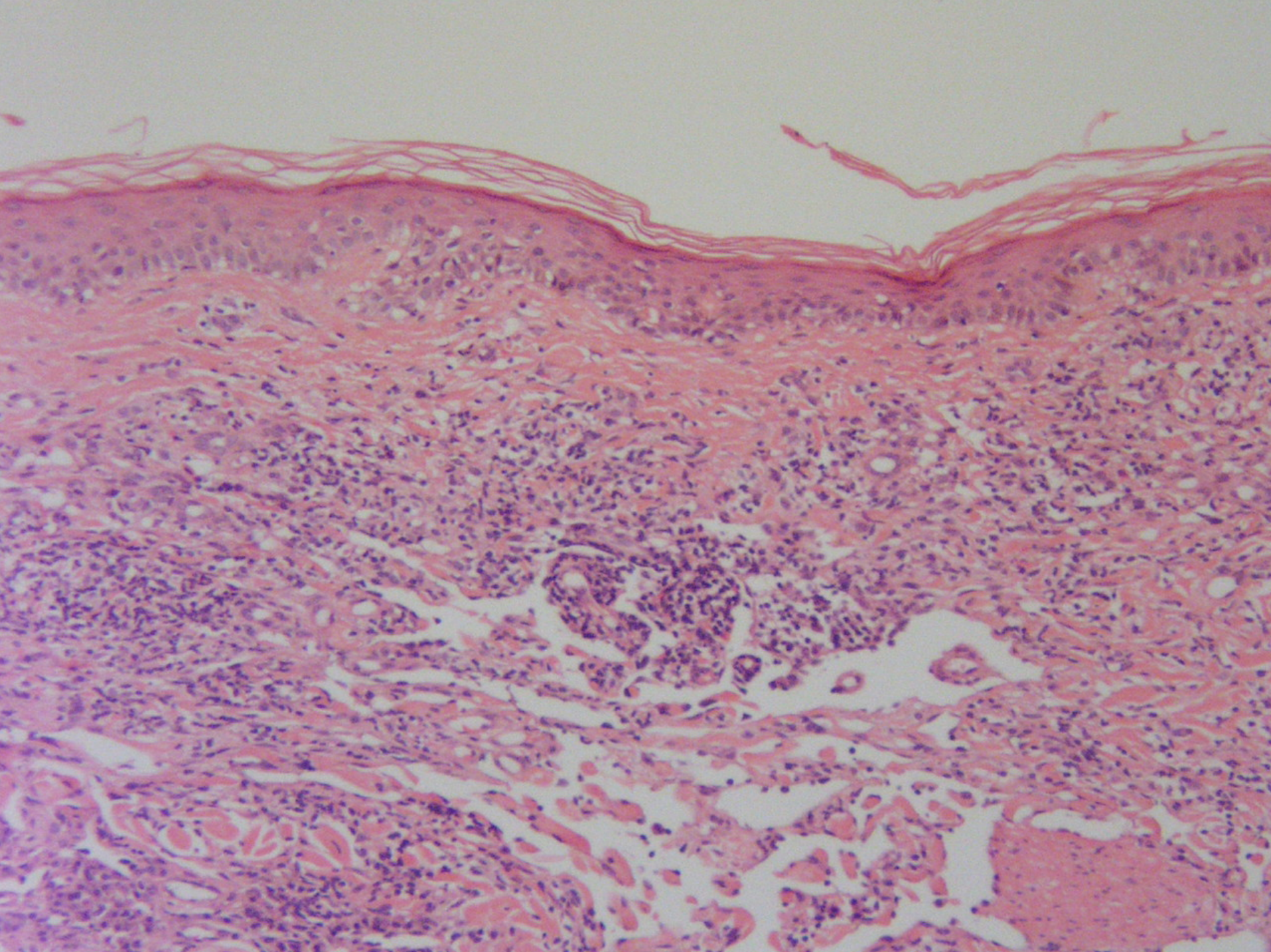
KS-Treatment

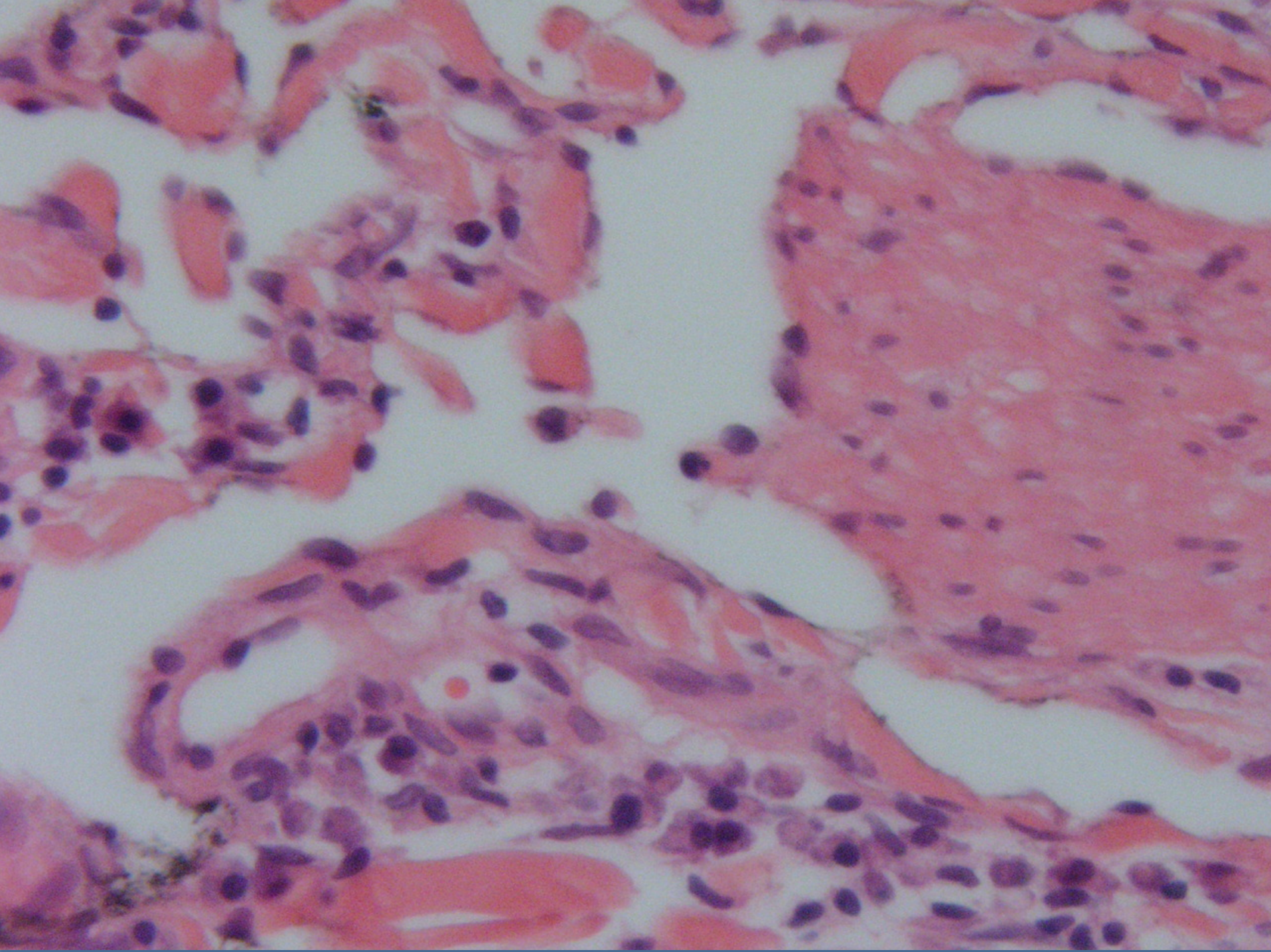
- Antiretroviral therapy HAART
- Local therapy
  Best suited for individuals who require palliation of locally advanced symptomatic disease (eg, radiation) or for individuals who have cosmetically unacceptable lesions
  - Radiation therapy
    - Most widely used and effective local therapy
    - Responses 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
  - Intralesional 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)



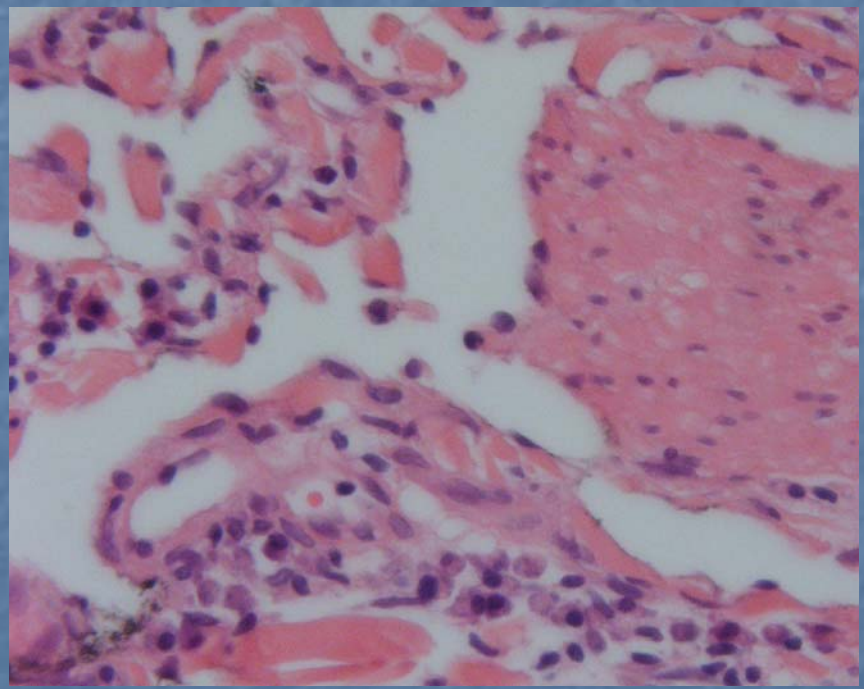




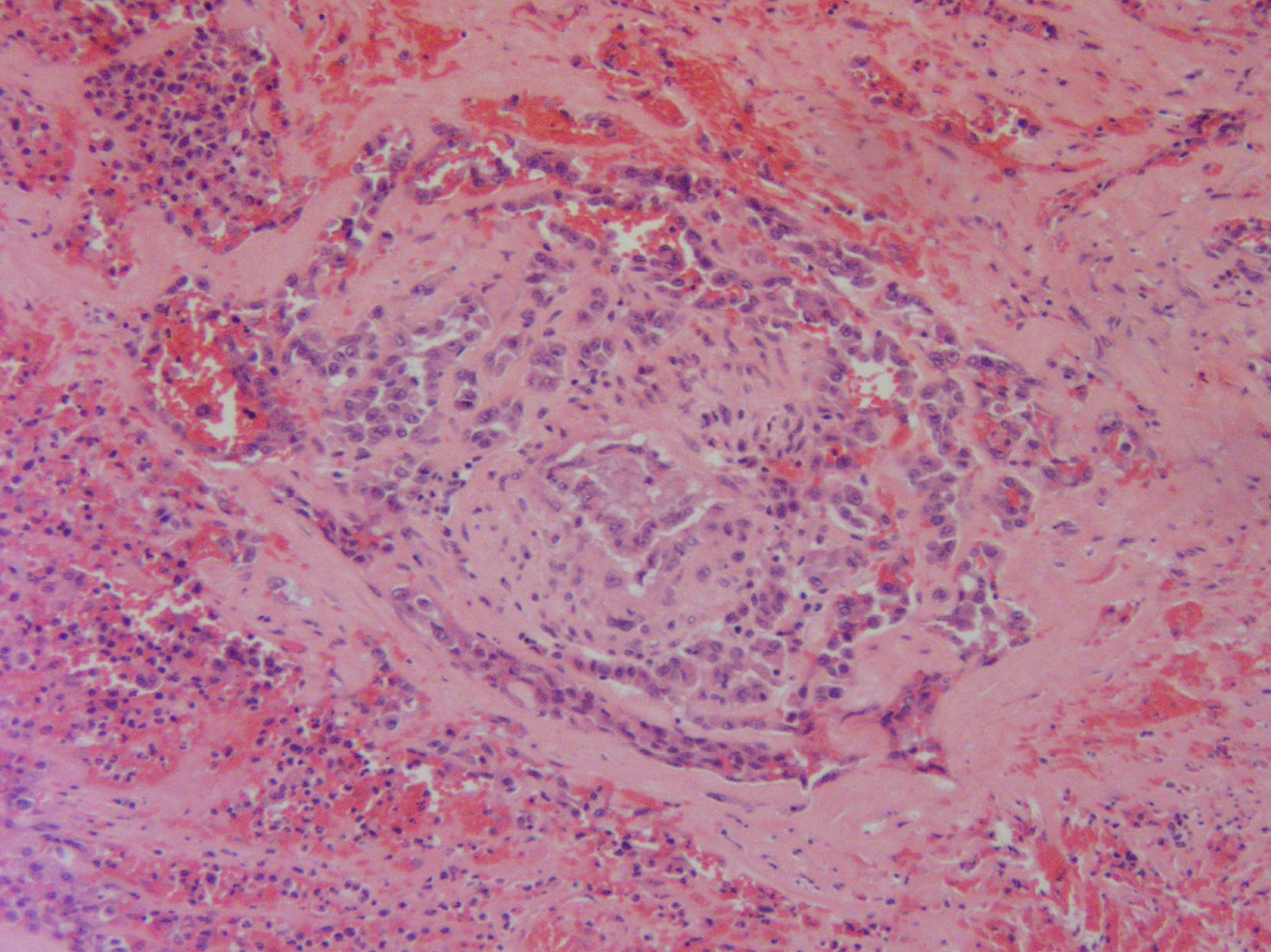
Cutaneous Angiosarcoma

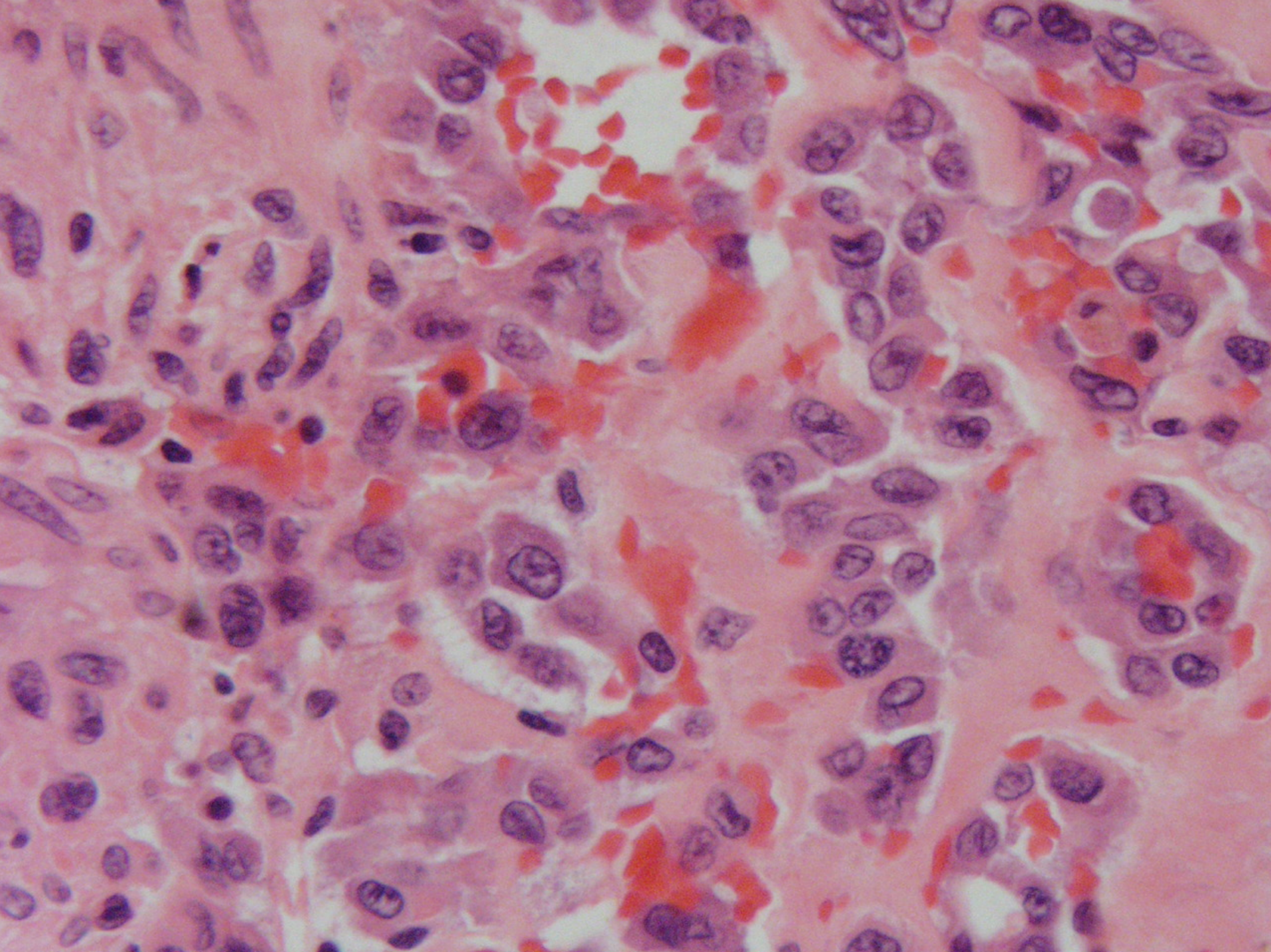
- Elderly males
- Head and neck
- Clinical features variable with enlarging bruise, cellulitis, edema, a blue-black nodule, or an unhealed ulceration
- Rarely angioneurotic edema and scarring alopecia

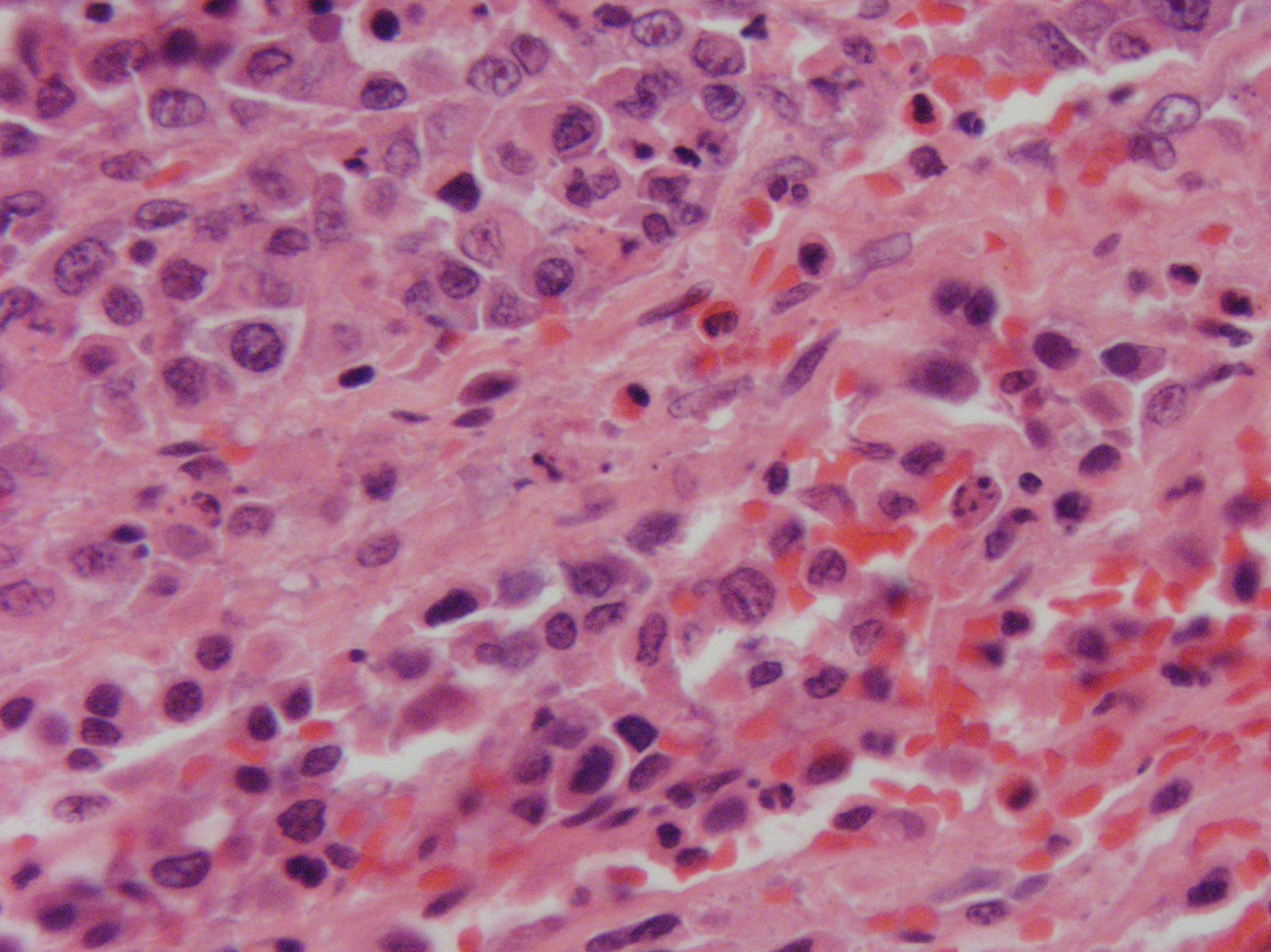
Angiosarcoma

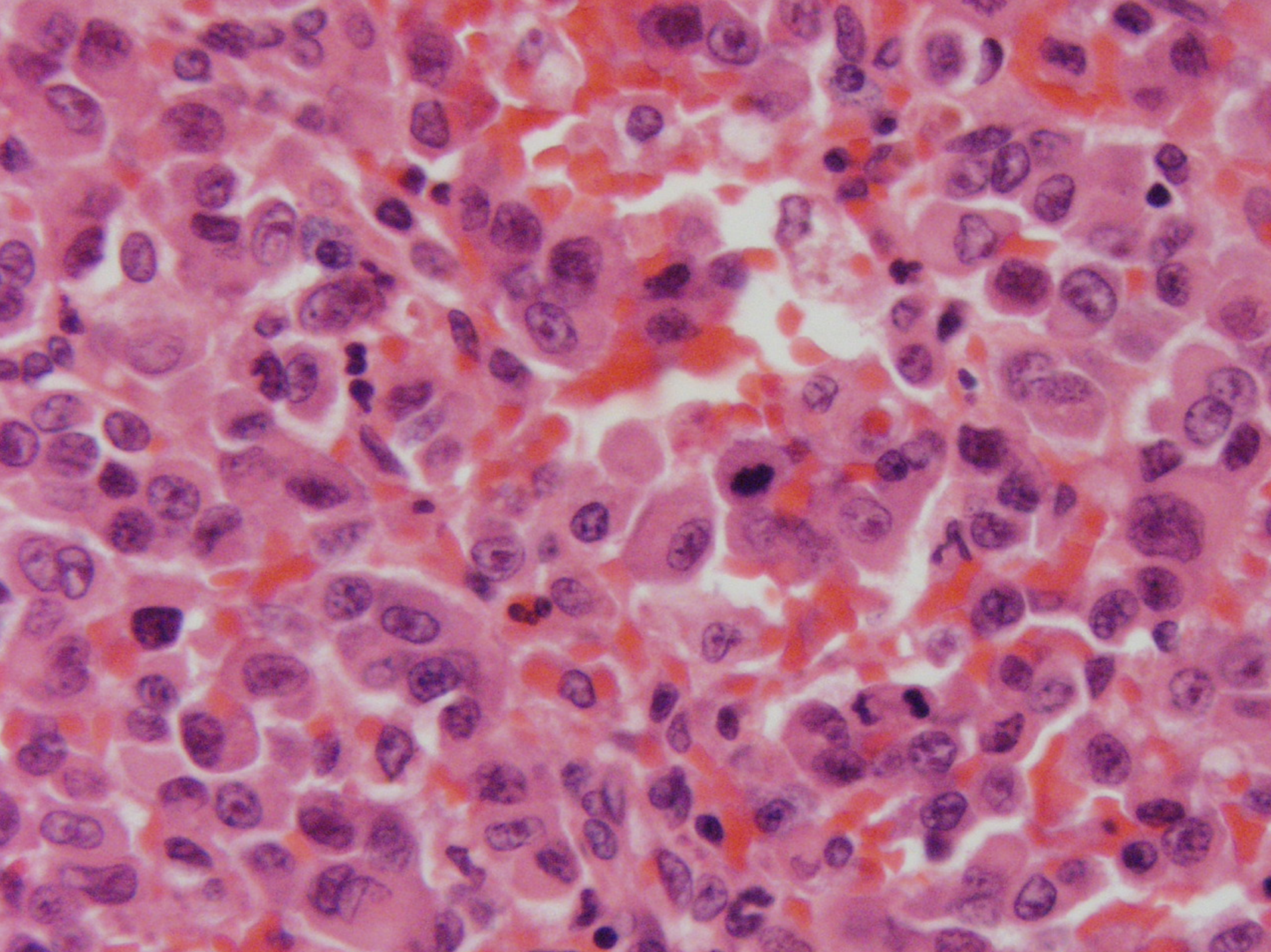


- Low-grade lesions
  - Vascular spaces lined by large plump endothelial cells that penetrate the stroma and papillary fronds of cells that project into the lumen
- Higher-grade lesions
  - More cellular, with atypical cells and abnormal mitoses.
- IPOX
  - Vimentin and CD31
    CD34 (74%)
    Cytokeratins (35%)







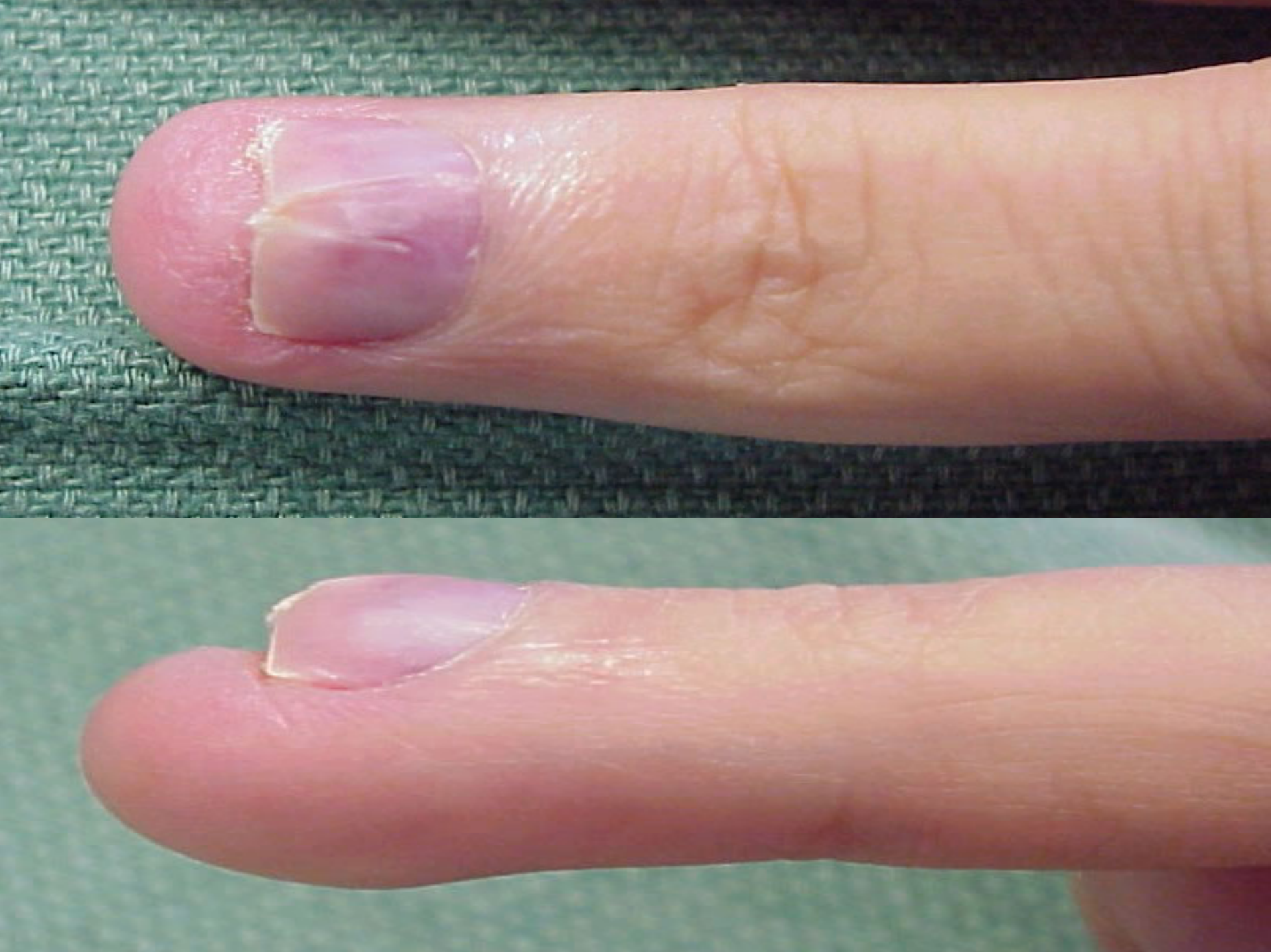


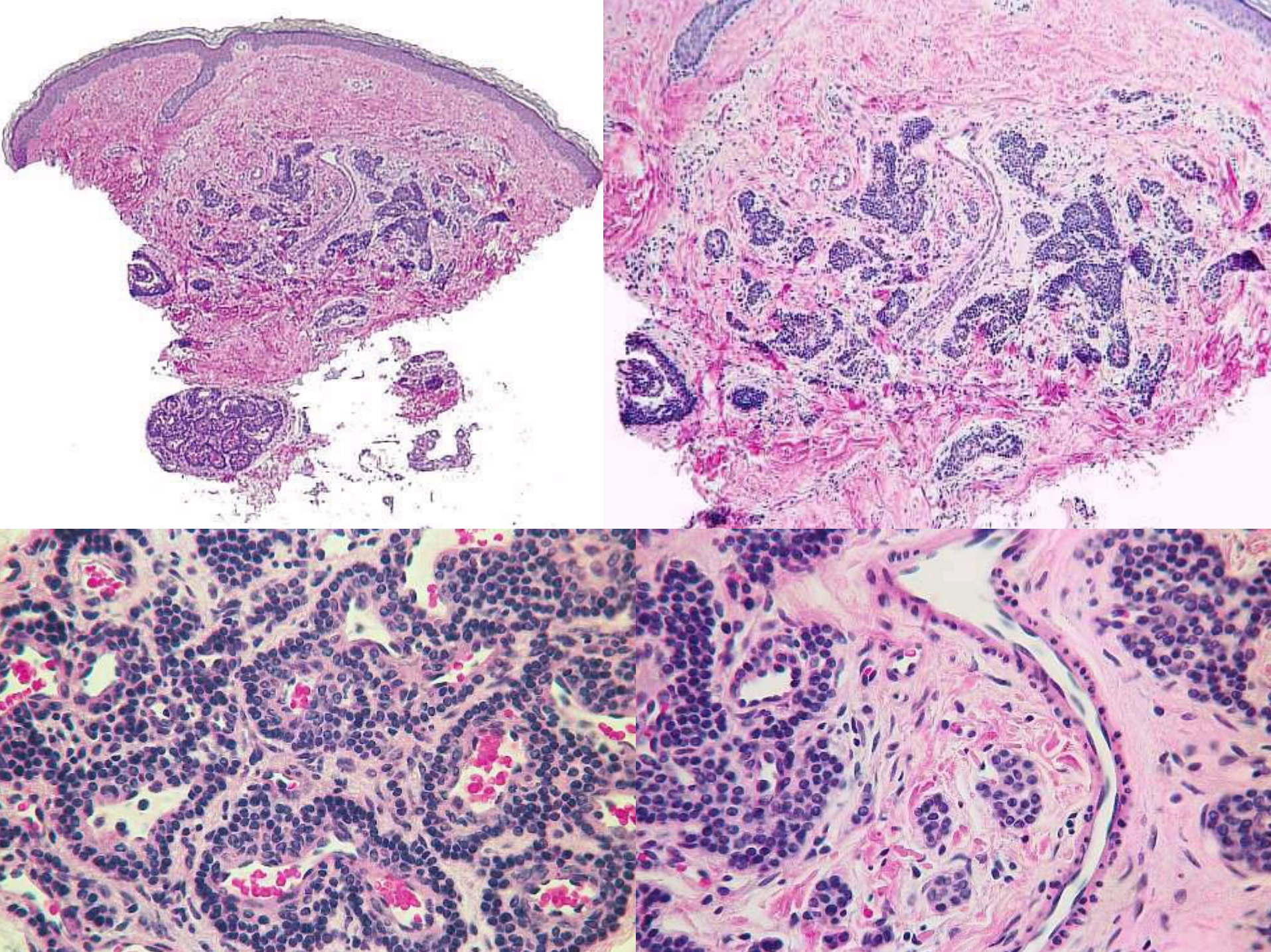
Angiosarcoma

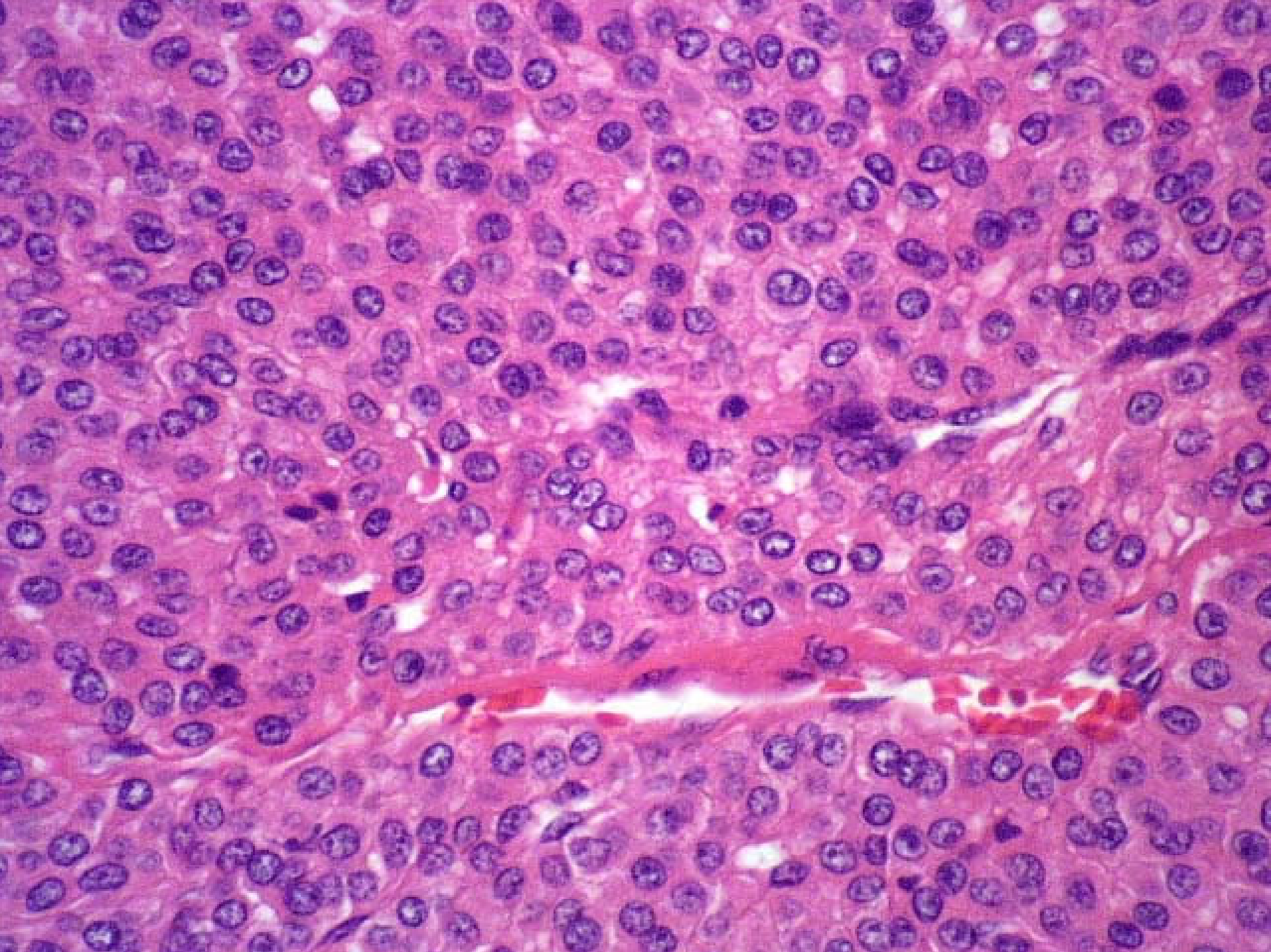
- Surgical treatment but contraindicated in tumors:
  - Extending into vital structures
  - Massive size
  - Multicentricity
- Primary excision of the scalp should be full-thickness, including the pericranium and, if indicated, the outer table of the cranial vault
  - Wide margins (at least 5 cm) on 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)







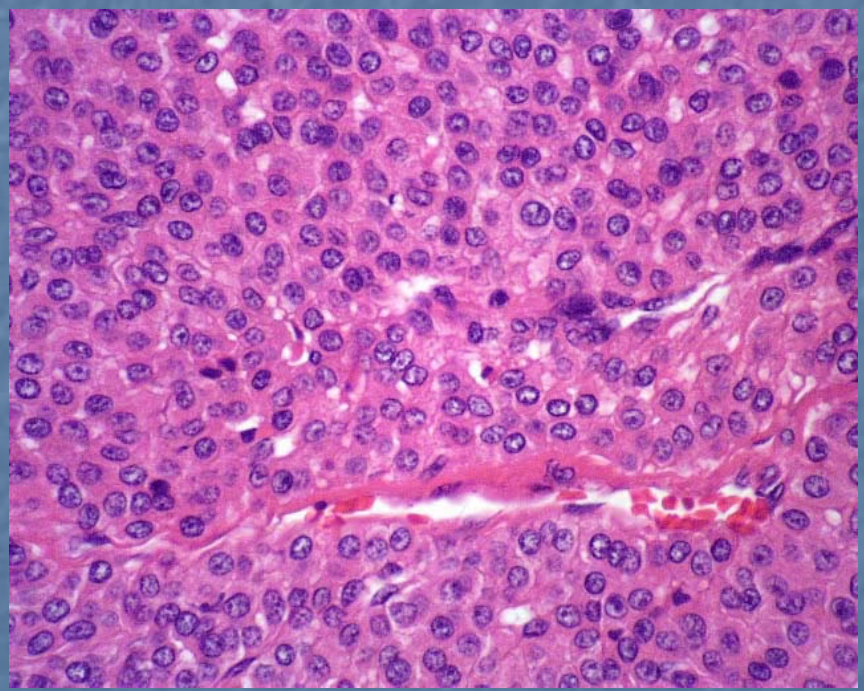
Glomus Tumor

- 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



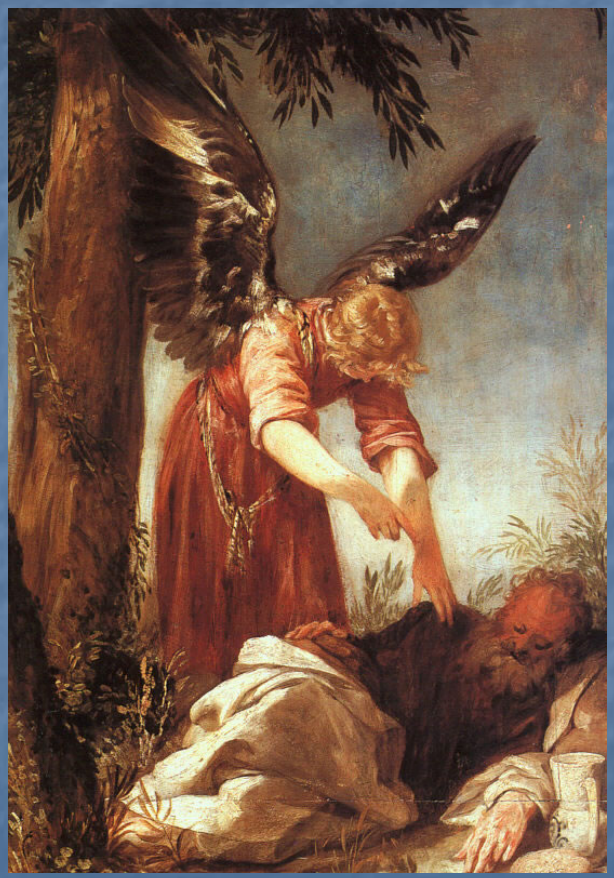
- Solid well-circumscribed nodules surrounded by a rim of fibrous tissue
- Endothelium-lined vascular spaces surrounded by clusters of glomus cells
- Glomus cells monomorphous round or polygonal cells with plump nuclei and scant eosinophilic cytoplasm
- Multiple lesions are less well circumscribed and 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
- **Symplastic 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 symplastic 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 symplastic glomus tumor, glomus tumor of uncertain malignant potential, or glomangiomatosis.

Am J Surg Pathol 2001;25:1-12

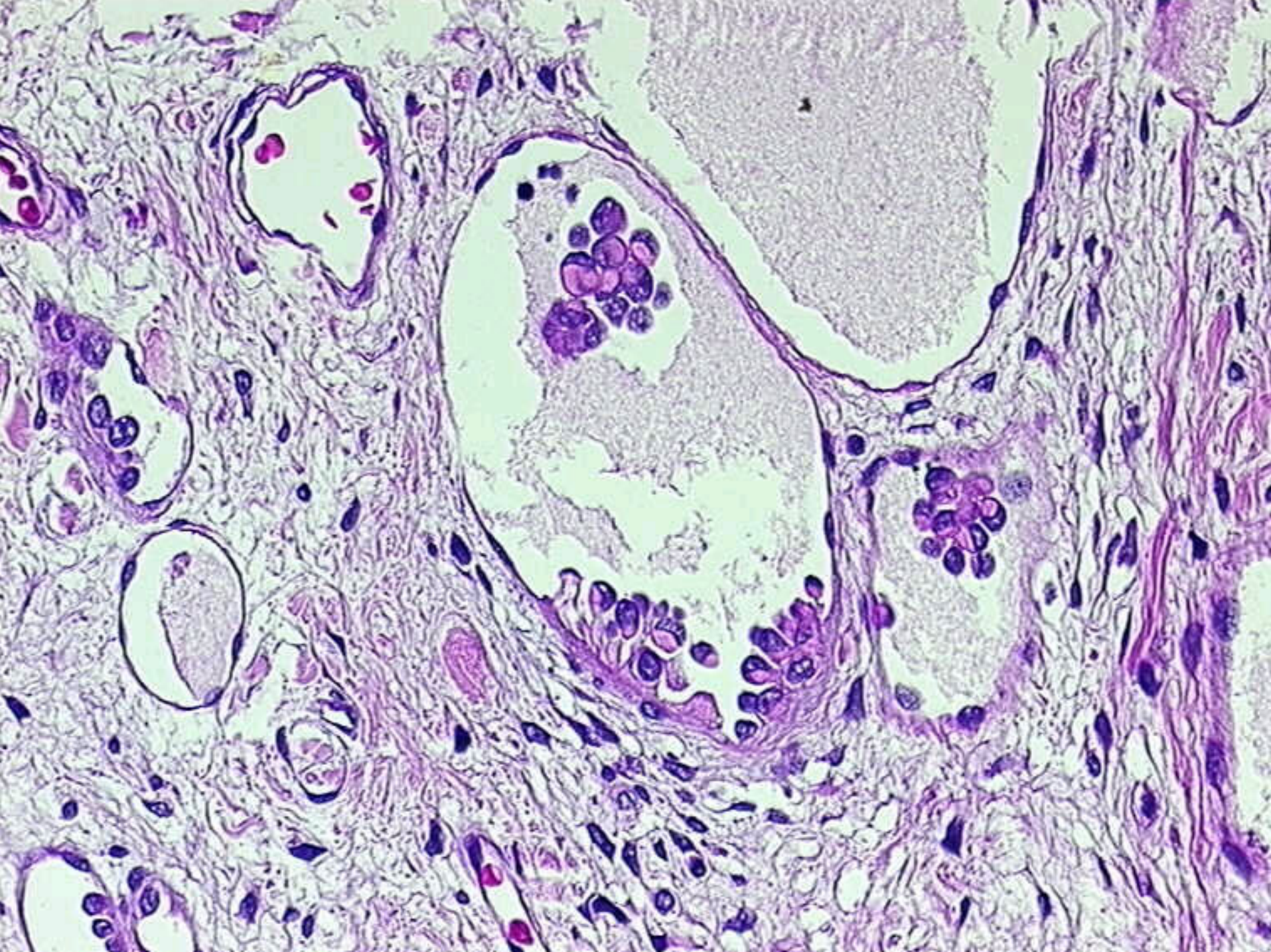
Painful Dermal Tumors

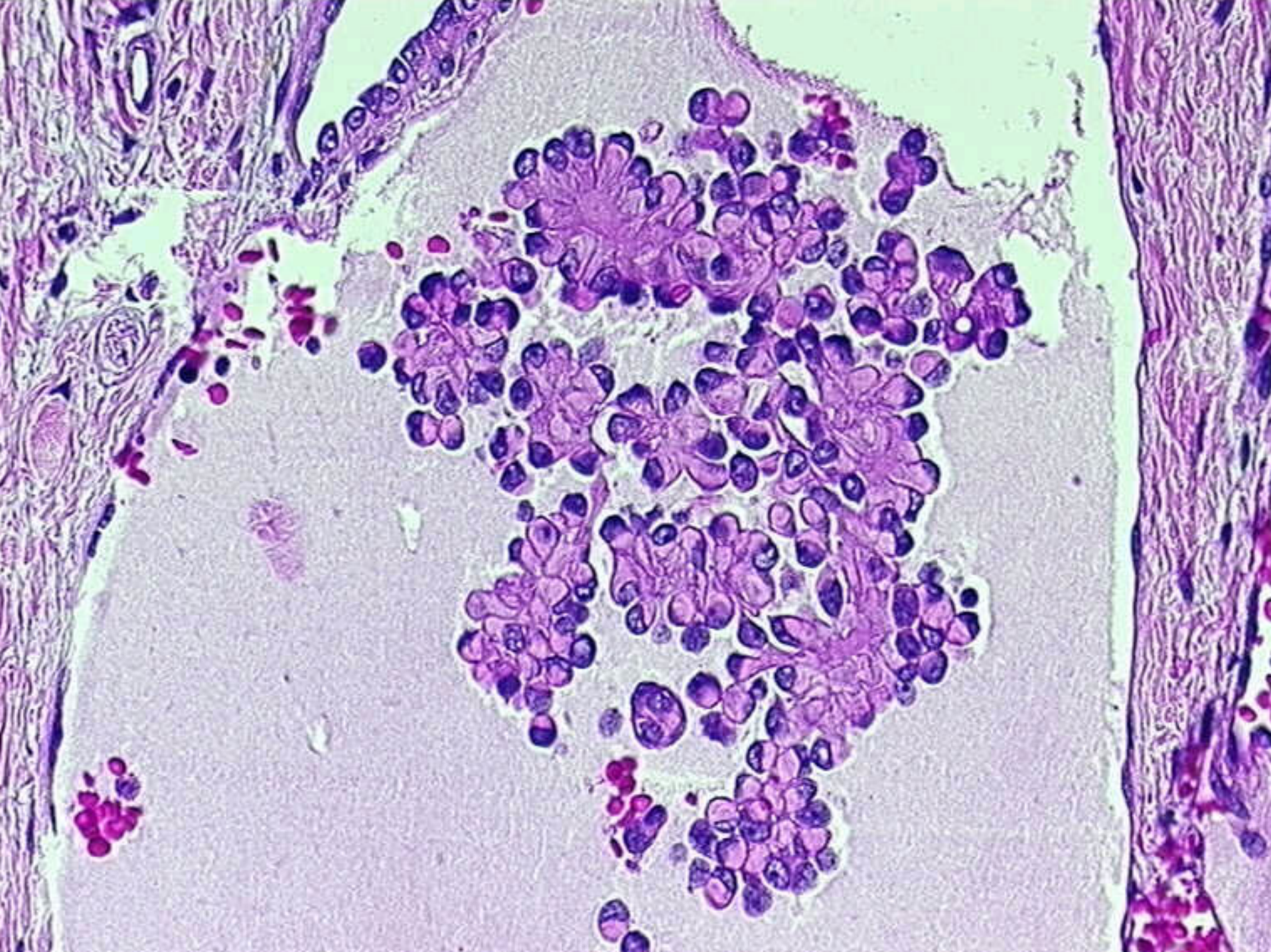


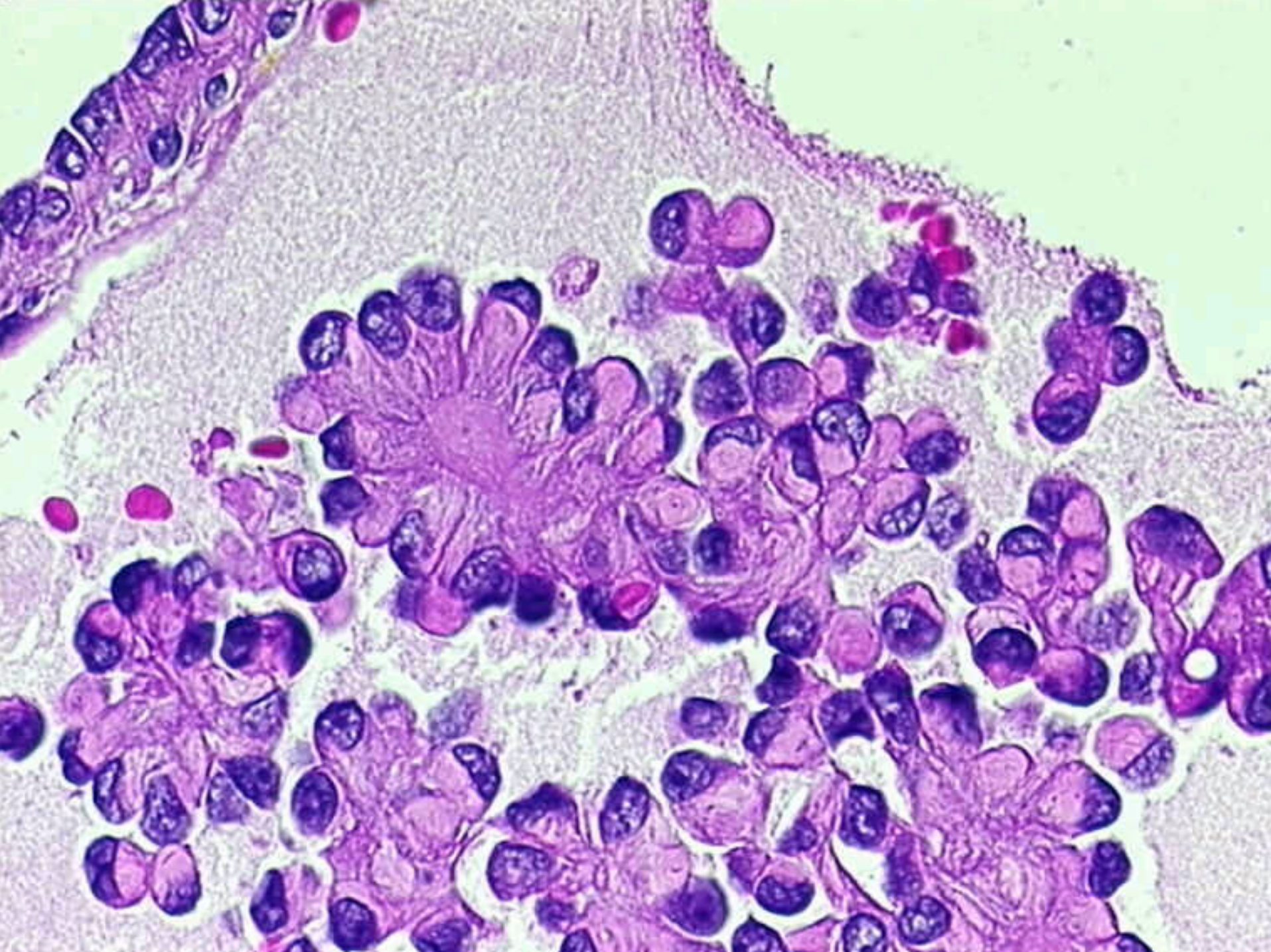
- **A**ngiolipoma
- **N**euroma
- **G**lomus Tumor
- **E**ccrine spiradenoma
- **L**eiomyoma

Painful Dermal Tumors

- **B**lue rubber bleb nevus
- **L**eiomyoma
- **E**ccrine poroma/eccrine spiradenoma
- **N**euroma
- **D**ermatofibroma/Dercum's disease (adiposis dolorosa)
- **A**ngiolipoma
- **N**eurilemoma
- **E**ndometrioma
- **G**lomus tumor
- **G**ranular 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

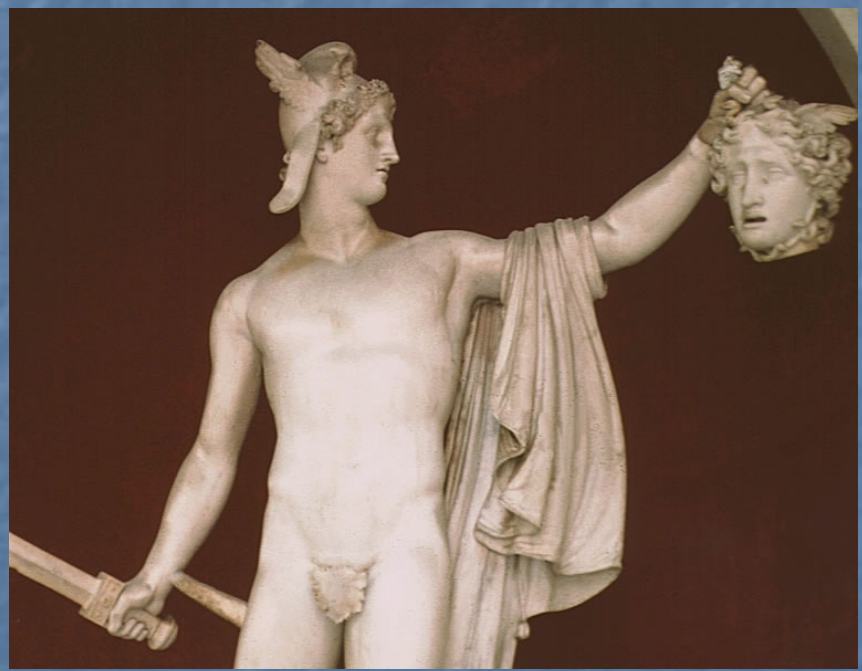
Dabska Tumor

- 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)