Genodermatoses Chap. 3: Disorders of Vascularization

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Genodermatoses is a clinical guide to genetic skin disorders, providing the key details of diseases, accompanied by visual illustrations. Chapter 3 focuses on diseases of vascularization with major dermatologic manifestations. The following are updates to the 2nd edition of the book found in primary journal articles, which are pending approval for the 3rd edition.

Sturge-Weber Syndrome

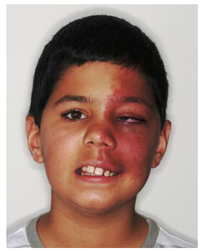
Pathogenesis:
- Hypothesis that capillary-venous malformations result from somatic mutations in fetal ectodermal tissues causes inappropriate control or maturation of capillary blood vessel formation

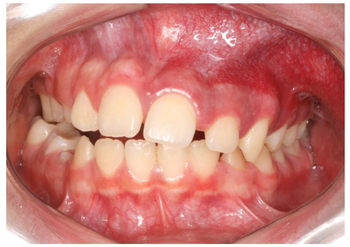
Key Features:
- Vascular malformations of the conjuctiva, episclera, choroid & retina
- Growth hormone deficiency & central hypothyroidism

Lab Data:
- CSF analysis, skull X-ray, angiography

Management:
- Referral to plastic surgeon, psychologist, psychiatrist, neuro-endocrinologist

Prognosis:
- Depends on leptomeningeal capillary-venous malformation; perfusion of cerebral cortex; severity of ocular involvement; age of onset of seizures





Klippel-Trenaunay Syndrome

Inheritance:
- 8q22.3; Potential association of E133K allele of VG5Q

Pre-natal diagnosis:
- Multiple, unrelated sonographic finding that may be related to KTS

Key Features:
- Triad of varicose veins, cutaneous capillary malformation, and hypertrophy of bone and soft tissue; CNS associations

Lab Data:
- Prenatal findings by U/S
- Evaluation of deep veins via duplex scanning contrast venography, U/S, nuclear MRI studies; arteriography; Imaging studies to rule out internal involvement

Cobb Syndrome

Pathogenesis:
- Possible that a somatic mutation in the neural crest or the cephalic mesoderm can produced arterial or venous metameric syndromes

Lab Data:
- Perform lumbar puncture to rule out infectious etiology

Management:
- Referral to interventional radiologist

Diffuse Neonatal Hemangiomatosis

Management:
- Usually surgical
- Cyclophosphamide may be needed if corticosteroid therapy is unresponsive

Beckwith-Wiedemann Syndrome

Inheritance:
- 5q35.2-q35.3; 11p15.5; 11p15.4

Prenatal Diagnosis:
- CVS/amniocentesis; U/S and measurement of maternal serum AFP

Clinical Features:
- Renal anomalies: medullary dysplasia, duplicated collecting system, nephrocalcinosis, medullary sponge kidney, cystic changes, nephromegaly
- CNS: brain abnormalities

Lab Data:
- Airway sufficiency and feeding ability in presence of macroglossia
- CXR evaluation, comprehensive cardiac evaluation

Management:
- Macroglossia related; Orthopedic surgeon; Pediatric oncologist

Prognosis:
- Increased risk for mortality due to complications of prematurity, macroglossia, hypoglycemia, tumors and, rarely, cardiomyopathy.

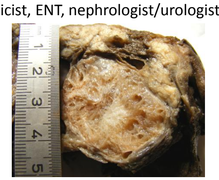
Von Hippel-Lindau Syndrome

Inheritance:
- 11q13.3: cyclin D1 gene

Key Features:
- Endolymphatic sac tumors of the middle ear
- Serous cysadenomas and neuroendocrine tumors of the pancreas
- Papillary cystadenomas of the epididymis and broad ligament

Lab Data:
- clinical signs of ELSTs; measurement of urinary catecholamine metabolites, urinalysis; regular ophthalmologic check-up, audiology assessment

Management:
- Referral to geneticist, ENT, nephrologist/urologist, endocrinologist



Cutis Marmorata Telangiectatica Congenita

Key Features:
- Neurologic abnormalities

Differential Diagnosis-
- KTS; Nevus Anemicus

Lab Data:
- Physical exam

Management:
- Consultation with orthopedist and/or neurosurgeon

Maffucci Syndrome

Inheritance:
- Unsure about role of PTHR1
- Associated somatic mutations in the isocitrate dehydrogenase-1 and -2 genes

Key Features:
- Potential hand manifestations and GI involvement

Differential Diagnosis:
- Kaposi Sarcoma and KTW Syndrome

Lab Data:
- Development of chondrosarcomas; CT and MRI

Hereditary Hemorrhagic Telangiectasia Syndrome

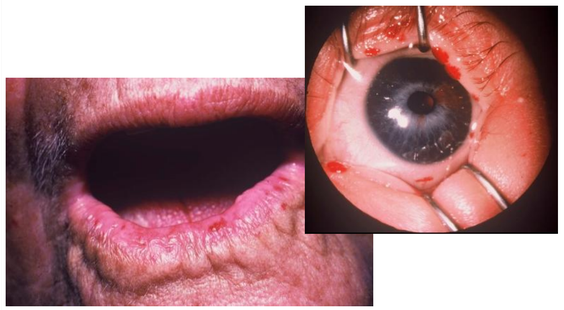
Inheritance:
- 9q34.11 (HHT1); 12q13.13 (HHT2); 5q31.3-q32 (HHT3); 7p14 (HHT4)

Key Features:
- Cerebral AVMs; Pancreatic involvement; Hepatic involvement

Differential Diagnosis:
- Pediatric syphilis; rosacea; Rothmund-Thomson Syndrome

Lab Data:
- Urinalysis, coagulation profile, skin biopsy findings

Management:
- Referral to cardiologist, interventional radiologist, transplant surgeon



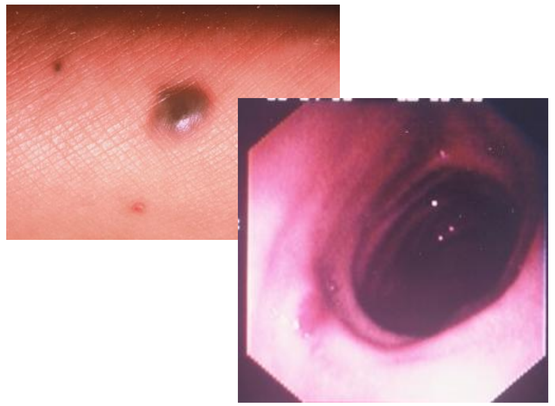
Blue Rubber Bleb Nevus Syndrome

Differential Diagnosis:
- Familial glomagiomatosis; Kaposi Sarcoma; KTW Syndrome, mucosal venous malformation syndrome

Lab Data:
- Urinalysis; Radiography and CT scans; Tc-99m-labeled RBC imaging

Management:
- Orthopedic consultation; Genetic testing/counseling
- Periodic GI and hematologic surveillance studies

Lab Data:
- Urinalysis; Radiography and CT scans; Tc-99m-labeled RBC imaging



Kasabach-Merritt Syndrome

Differential Diagnosis:
- Immune thrombocytopenic purpura
- Arterial vascular malformations; consumption coagulopathy, KTW Syndrome, Teratomas and other germ cell tumors

Lab Data:
- CBC count with differential, reticulocyte count, platelet count & peripheral smear
- D-dimer levels
- Appropriate radiographs, CT scans and MRIs

Management:
- Much research about medications
- Beneficial effect of propanol, pentoxifylline, dipyridamole
- Chemotherapy (vincristine, cyclophosphamide, actinomycin D) in some patients
- Issues with interferon alpha
- Tx include corticosteroids, interferon alpha, surgery, embolization

Proteus Syndrome

Inheritance/Pathogenesis:
- 14q32.3; somatic activating mutation in AKT1 gene

Key Features:
- More CNS/neurologic abnormalities; cerebriform connective tissue nevus; cystic lung abnormalities

Lab Data:
- Coagulation workup: patients are at increased risk for DVT and PE

Management:
- Hematology & pulmonary consult

PHACE Syndrome

Pathogenesis
- Timing of morphogenesis errors occur between 3-12 weeks of gestation
- Many elements of disease could be due to abnormality of cell proliferation and apoptosis

Key Features:
- Association of CNS abnormalities with developmental delays, motor delays and pituitary dysfunction
- Endocrinologic abnormalities reported in a small number of patients
- Sternal clefting/supraumbilical raphe
- Association of hearing loss

Lab Data:
- MRI with head/neck angiography
- Hearing evaluation

Management:
- Referral to neurologist

Bibliography

Spitz, Joel L. *Genodermatoses*. 2nd ed. Philadelphia, PA: Lippincott Williams & Wilkins, 2004. Print.