Borderline and Malignant Vascular Lesions

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ECP-Nice 2019
Classification (Soft tissue tumors, WHO 2013)

- Intermediate (*Locally aggressive*)
  - Kaposiform Hemagioendothelioma

- Intermediate (*Rarely metastasizing*)
  - Retiform hemangioendothelioma
  - Papillary intralymphatic angioendothelioma
  - Composite hemangioendothelioma
  - Kaposi sarcoma
  - Pseudomyogenic hemangioendothelioma

- Malignant
  - Epithelioid Hemangioendothelioma
  - Angiosarcoma
A practical, morphology based approach

Predominant spindle cell lesions

Predominant vasoformative lesions

Predominant epithelioid cell lesions

...Mixed

...and non-vascular mimics
# Borderline and Malignant Vascular lesions

## Spindle cell predominant

<table>
<thead>
<tr>
<th>Clinical features</th>
<th>Kaposiform HE</th>
<th>Kaposi Sarcoma</th>
<th>Kaposiform LE</th>
<th>Angiosarcoma</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Infants-1st</td>
<td>Endemic</td>
<td>Infants</td>
<td>Rare</td>
</tr>
<tr>
<td></td>
<td>M/F=1:1</td>
<td>latrogenic</td>
<td>Lung/skin</td>
<td>Skin (associated to syndromes)</td>
</tr>
<tr>
<td></td>
<td>extremities, trunk, retroperitoneum, head and neck</td>
<td>Skin, lymphnodes, intrathoracic, oral lesions.</td>
<td></td>
<td>Soft tissue</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Liver</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Other</td>
</tr>
<tr>
<td>Histology/growth pattern</td>
<td>Infiltrative/sheets of spindle cells with thin-walled vessels</td>
<td>spindle cells with slit like vessels containing red cells</td>
<td>scattered small spindle cell aggregates</td>
<td>fascicles of spindle cells with cytologic atypia, necrosis</td>
</tr>
<tr>
<td>Vasoformation</td>
<td>nests of vascular epithelioid cells with thrombi, abnormal lymphatic spaces at the periphery</td>
<td>yes (dilated vascular channels)</td>
<td>Vascular lymphatic channels</td>
<td>focal</td>
</tr>
<tr>
<td>Nuclear atypia</td>
<td>minimal</td>
<td>minimal</td>
<td>no</td>
<td>yes</td>
</tr>
<tr>
<td>IHC</td>
<td>CD31+, KHSV8- D240</td>
<td>CD31+, D2-40+, KHSV8+</td>
<td>D2-40</td>
<td>VIII, CD31, and CD34</td>
</tr>
<tr>
<td>Genetics</td>
<td>GNA14 (1 case)</td>
<td></td>
<td>BAD, TSC1</td>
<td></td>
</tr>
<tr>
<td>Behaviour</td>
<td>70% KMF, 20% DOD</td>
<td>1yr OS: 71%</td>
<td>OS: 34%</td>
<td>OS: 25-35%</td>
</tr>
</tbody>
</table>
Kaposiform Hemangioendothelioma

Multiple coalescing lobules of capillaries composed of spindled cells endothelial cells and capillary. Platelet microthrombi, hemosiderin, and extravasated RBCs.
Kaposiform Hemangioendothelioma

- Rare (0.07/100,000 children/yr)
- Onset at birth, may appear pre or post-natally. Rare, adult cases.
- M/F=1:1
- Site: extremities, trunk, retroperitoneum, head and neck.
- Unifocal; multifocal or regional peri-nodal soft tissue involvement possible.
- May regress within 2 yr of life, with atrophic scarring and progressive improvement
- Death in 10-30% of cases

Courtesy from Maya El Hacheim, Dermatology Ospedale Bambino Gesu, Rome
Kaposiform hemangioendothelioma: atypical features and risks of Kasabach-Merritt phenomenon in 107 referrals

Stacy E. Croteau, MD, MMS,
Division of Pediatric Hematology/Oncology, Children’s Hospital Boston

Abstract

Objective—To examine the presentation characteristics of patients with kaposiform hemangioendothelioma (KHE) to describe the spectrum of disease and risk factors for Kasabach-Merritt phenomenon (KMP).

Study design—Retrospective review of 163 patients referred to the Vascular Anomalies Center at Children’s Hospital Boston for KHE between 1991 and 2009 identified 107 patients with sufficient data for inclusion.

Results—The prevalence of KHE in Massachusetts is approximately 0.91/100,000 children. KHE manifested in infancy in 93% of cases; 60% as neonates. Common presenting features included enlarging cutaneous lesion (75%), thrombocytopenia (56%), and musculoskeletal pain or decreased function (23%). Cutaneous KHE favored the extremities, especially overlying joints. In our cohort 71% developed KMP (11% after initial presentation), and 11% of patients lacked cutaneous findings. Retroperitoneal and intrathoracic lesions, though less common, were complicated by KMP in 85% and 100% of cases, respectively. Compared with superficial lesions, KHE infiltrating into muscle or deeper was 6.3-fold more likely to manifest KMP, and 18-fold higher if retroperitoneal or intrathoracic. KHE limited to bone or presenting after infancy did not manifest KMP.

Conclusion—An enlarging lesion is the most common presenting feature of KHE in infancy. Older patients with KHE or those lacking cutaneous manifestations present with musculoskeletal complaints or atypical symptoms. The risk of KMP increases dramatically when tumor infiltrates muscle or when KHE arises in the retroperitoneum or mediastinum.
KHE-Splenic mass, 1yr old, male

UPMC-Children’s Hospital Pittsburgh, courtesy of dr M. Reyes-Mugica/R.
A fatal case: F, 3 mth old

- Dyspnea, failure to thrive, fever,
- Lab findings: Hb 9, Plts 36000;
- Blood in the stools
- CT scans: hypervascular tissue in mediastinum, retroperitoneum (around the aorta and celiac region with bilateral extension to kidneys)
- Surgery, CT
- Death few months later
Hyaline bodies (A)

Isolated atypical cells (C)

Glomeruloid nests (B)

Lymphatics at periphery (D)
What’s new? Genetic alterations in KHE

- Recurrent somatic activating mutations in GNA14 (3 cases: KHE, Tufted Angioma, Congenital Hemangioma)  

- Chromosomal Translocation t(13;16) (q14; p13.3)  
Differential Diagnosis: Kaposiform Lymphangioendotheliomatosis

- Rare disease with onset in childhood and features of malformation and neoplasia.
- Respiratory symptoms (50%).
- Mediastinal involvement (100%), pericardial (70%) and/or pleural effusions (85%).
- Extrathoracic disease:
  - bone, spleen, abdominal viscera, peritoneum, integument, extremities. Skin involvement rare
- OS: 34%. Mean interval diagnosis-death: 2.75 yr
- Histology/IHC
  - Spindled cells within anomalous pulmonary lymphatic channels
  - Spindled cells with parallel arrangement forming dispersed, clusters or anastomosing strands/sheets.
  - D240 positive spindled cells.

Kaposi Sarcoma: Epidemiologic classification

- Classic: elder men, indolent
- African (endemic): younger African men and children from central Africa
  - Clinical variants:
    - nodular clinically indolent
    - aggressive with large invasive cutaneous tumors involving soft tissue and bone
    - endemic-pediatric variant presenting as lymphadenopathy
- Immunodepression-associated (transplant patients, chemotherapy and immunosuppressive therapy)
- Epidemic (HIV / AIDS-associated)

Pediatric KS, regardless of the epidemiologic variant, is different from adult with increased risk for disseminated and progressive disease
Mechanisms involved in KHSV oncogenicity

Kaposi Sarcoma in transplant-recipient children

15 yr old girl
history of lung transplant for cystic fibrosis
8 mth later: lung nodules, pleural effusion
lymph node enlargement
no skin lesions
Donor KSHV8 negative

Courtesy of L. Galluzzo-Mutti
Pediatric Transplantation. 2019;23:e13311.
Disseminated viseral Kaposi sarcoma in transplant recipient

CD34

LANA1
Transplant associated KS

- KS in solid organ transplant recipients 500 times higher than in the general population (6% of solid organ recipients)
- Higher incidence in liver transplant recipients compared to heart or kidney recipients
- 70% diagnosed within 2 yr from transplant
  - related to reactivation of virus in recipients
  - seroconversion from negative donors (10/28 seronegative pts in Italian series)
- Skin involvement in 80% of cases, visceral involvement in 20%.
- Median time from transplantation to diagnosis: 1.5 years.
- More aggressive clinical course
Cutaneous Kaposi Sarcoma

**Patch stage (Red/purple macules or patches)**
Dilated vascular channels dissecting through dermal collagen
Very subtle in early lesions

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Diagnostic Pathology 2008, 3:31
BM transplanted, KHSV8 IHC
Cutaneous Kaposi Sarcoma

**Plaque stage (Thickened red/purple/brown plaques)**
More extensive infiltrative slit-like vascular channels
Infiltrative proliferation of spindled endothelial cells destroying eccrine coils

**Tumor stage (Nodules)**
Nodules composed of intersecting fascicles of uniform spindle cells
Intervening blood filled spaces between spindle cells
Slit-like spaces, Sieve-like spaces
Intracytoplasmic hyaline globules may be seen
MIMICS OF SPINDLE CELL VASCULAR LESIONS
Infantile fibrosarcoma
Infantile fibrosarcoma of the hand associated with coagulopathy.

BACKGROUND:
Large congenital neoplasms of the extremities may be associated with coagulopathies and significant hemorrhage in the neonatal period. At times, the differences between coagulation derangements can be very subtle, leading to errors in diagnosis. Infants with vascular lesions and coagulopathies are often found to have the Kasabach-Merritt phenomenon, which is a platelet-trapping coagulopathy. However, other neoplasms or vascular malformations can be accompanied by disseminated intravascular coagulation. It is important to obtain accurate diagnoses of the neoplasm and the coagulopathy because the treatments of similar-appearing tumors and coagulopathies can be markedly different.

METHODS:
The authors report the case of a newborn with a congenital tumor of the left hand that was accompanied by a coagulopathy that caused significant bleeding.

RESULTS:
A presumption was made by the neonatal critical care physicians and hematologists that the infant had a kaposiform hemangioendothelioma along with the Kasabach-Merritt phenomenon. However, steroid treatment did not reduce the size of the mass or correct the coagulopathy. Only after obtaining consultation with a hand surgeon and a tissue diagnosis was it learned that the patient had an infantile fibrosarcoma that was accompanied by disseminated intravascular coagulation. Limb-sparing resection of the lesion along with chemotherapy markedly improved the patient’s condition.

CONCLUSIONS:
Large congenital neoplasms presenting with attendant bleeding diatheses must be rapidly and accurately diagnosed with both a biopsy-proven tissue diagnosis and a hematologic characterization of the nature of the coagulopathy. The differential diagnosis of a vascular-appearing mass in the extremity can be subtle, and presumptive diagnosis, as occurred in this case, can lead to incorrect or delayed treatment. Specifically, kaposiform hemangioendothelioma must be differentiated from infantile fibrosarcoma. The principles of infantile fibrosarcoma treatment are limb-sparing resection and chemotherapy.

Glomeruloid structures

Congenital mass in the temporal region (subcutis)
Prominent vascular network and mixed inflammatory component (Case 5)
Glomeruloid structures (D2-40 pos)
Inflammatory Myofibroblastic Tumor
<table>
<thead>
<tr>
<th>Clinical features</th>
<th>PILA</th>
<th>Papillary Lymphangioendotheliomatosis</th>
<th>Retiform HE</th>
<th>Angiosarcoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>75% children</td>
<td>infants, thrombocytopenia and GI bleeding during infancy.</td>
<td>skin, single &lt;3 cm association with lymphedema, Milroy S. 40 cases young adults, children</td>
<td>mostly liver, skin</td>
<td></td>
</tr>
<tr>
<td>Histology/growth pattern</td>
<td>Intercommunicating thin-walled vessels intraluminal papillary projections with hobnail cells matchstick-like pattern.</td>
<td>Thin-walled dilated vessels lined by hobnailed endothelial cells with intraluminal papillary projections.</td>
<td>branching vessels lined by hobnail endothelial cells</td>
<td>branching vessels, lined by atypical endothelial cells</td>
</tr>
<tr>
<td>Nuclear atypia</td>
<td>yes</td>
<td>minimal</td>
<td>minimal</td>
<td>yes</td>
</tr>
<tr>
<td>IHC</td>
<td>CD31, ERG. CD34PROX1+ D2-40, VEGFR-/+</td>
<td>CD31+, D2-40-, LYVE+</td>
<td>CD31, CD34, ERG, PROX1+ D2-40, VEGFR-/+</td>
<td>VIII, CD31, and CD34</td>
</tr>
<tr>
<td>Genetics</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Behaviour</td>
<td>locally aggressive, rare mets</td>
<td>Prognosis: variable</td>
<td>multiple local recurrences (60% of cases) local lymph nodes mets</td>
<td>OS:25-35%</td>
</tr>
</tbody>
</table>
Papillary Intralymphatic Angioendothelioma (PILA)
(AKA Dabska tumor)
Papillary Intralymphatic Angioendothelioma

- Less than 50 cases reported
- 75% in children, occasionally congenital
- Skin and superficial soft tissues (head and neck, trunk, or extremities)
- Also reports in: spleen, tongue, testis
- 4 cases in bone (1 in a 1 yr old, others in adults, one multifocal)
- Slow growth
- May arise in a pre-existing lymphatic malformation
- Clinical course benign:
  - Local recurrence in up to 40%.
  - Lymph node involvement and lesions at distant sites rare.
Intercommunicating thin-walled vessels

Close resemblance to retiform hemangioendothelioma.

Hobnail endothelial cells forming intraluminal papillary projections.

Focal rosette-like or matchstick-like pattern.

Hyaline papillary stromal cores (collagen type 4).

Lymphocytic inflammation and fibrosis frequent

Necrosis absent
Papillary Intralymphatic Angioendothelioma (Dabska tumor)

- Intercommunicating thin-walled vessels
- Close resemblance to retiform hemangioendothelioma.
- Hobnail endothelial cells forming intraluminal papillary projections
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Hyaline papillary stromal cores (collagen type 4)

Lymphocytic inflammation and fibrosis frequent
Necrosis absent
Papillary Intralymphatic Angioendothelioma (Dabska tumor)

Immunophenotype

SMA (pericytes)
CD31, CD34, and Fli-1 (Endothelial cells)
D2-40 and VEGFR-3 (Lymphatic component)
Retiform hemangioendothelioma

Very rare
Children/Young adults
Slowly growing mass
Extremities
Infiltrative, elongated branching vessels

Cuboidal endothelial cells
(similar to papillary intralymphatic angioendothelioma)
Differential Diagnosis
Multifocal lymphangioendotheliomatosis with thrombocytopenia (MLT)

Thin-walled dilated vessels lined by hobnailed endothelial cells with intraluminal papillary projections.

*Courtesy of M.Reyes-Mugica/A. Davis UPMC-Children’s Hospital of Pittsburgh*
Multifocal lymphangioendotheliomatosis with thrombocytopenia (MLT)

Previously reported as blue rubber bleb nevus syndrome, diffuse neonatal hemangiomatosis, hereditary hemorrhagic telangiectasia.

- **Different clinical setting**
- Varying degrees of thrombocytopenia and GI bleeding during infancy.
- Skin lesions: from telangiectatic macules (1-2 mm) to large tumors and gastrointestinal tract lesions.
- Other organs involved: lung, synovium, muscle, bone, bone marrow, spleen, brain.
- Prognosis: variable, reported fatal cases and long term survivors.
7 weeks old male with blueberry muffin rash (legs, back, abdomen, scalp, groin folds and upper lip), thrombocytopenia

Thin-walled dilated vessels in the reticular dermis and subcutis

Courtesy of M.Reyes-Mugica/A. Davis UPMC-Children’s Hospital of Pittsburgh
Multifocal lymphangioendotheliomatosis with thrombocytopenia (MLT)

Skin histology

**CD31**  
**LYVE-1**

Immunophenotype: LYVE-1 +

*Courtesy of M.Reyes-Mugica/A. Davis UPMC-Children’s Hospital of Pittsburgh*
## Borderline and Malignant Vascular lesions

Epithelioid cell predominant: Differential diagnosis

<table>
<thead>
<tr>
<th></th>
<th>Pseudomyogenic Hemangiendothelioma</th>
<th>Epithelioid Hemangiendothelioma</th>
<th>Epithelioid Angiosarcoma</th>
<th>Epithelioid Sarcoma</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Clinical features</strong></td>
<td>Males. Young adults.</td>
<td>No age or sex predilection.</td>
<td>Males. Mostly older adults.</td>
<td>Males. Young adults.</td>
</tr>
<tr>
<td><strong>Histologic features</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Vasoformation</strong></td>
<td>Not present.</td>
<td>Frequent intracytoplasmic lumens.</td>
<td>Vascular channels.</td>
<td>Not present.</td>
</tr>
<tr>
<td><strong>Nuclear atypia</strong></td>
<td>Mild to moderate.</td>
<td>Mild to moderate.</td>
<td>Moderate to marked.</td>
<td>Mild to moderate.</td>
</tr>
<tr>
<td><strong>Immunohistochemistry</strong></td>
<td>CD34+, CD31+, Fli-1+, ERG+, FOsB+, CKs+, CAMTA1+, INI-1 retained.</td>
<td>CD34+, CD31+, Fli-1+, ERG+, FOsB-, CKs+, CAMTA1+, INI-1 retained.</td>
<td>CD34+ (50%), CD31+, Fli-1+, ERG+, FOsB-, CKs+, CAMTA1-, INI-1 retained.</td>
<td>CD34+ (50%), CD31+, Fli-1+ and ERG- (in most cases), FOsB-, CKs+, CAMTA1+, INI-1 lost.</td>
</tr>
<tr>
<td><strong>Genetics</strong></td>
<td>SERPINE1-FOsB fusion.</td>
<td>WWTR1-CAMTA1 fusion.</td>
<td>Complex cytogenetic aberrations.</td>
<td>Inactivation of suppressor gene SMARC1/INI1.</td>
</tr>
<tr>
<td><strong>Behavior</strong></td>
<td>Usually indolent, but with 60% of cases showing local or regional recurrences. Metastases are extremely rare.</td>
<td>Local recurrences, with metastases in 20%-30% of cases.</td>
<td>Local recurrences and metastases. More than 50% of patients die of disease.</td>
<td>High risk of local recurrences (75%) and metastases (45%).</td>
</tr>
</tbody>
</table>

Abbreviation: CKs, cytokeratins.
Synonym: epithelioid sarcoma-like hemangioendothelioma (due to its similarity to epithelioid sarcoma)

- Age: young adults and children
- Male predominance.
- Small size (1 to 3.5 cm).
- Cutaneous masses with involvement of multiple tissue planes at presentation (not uncommonly: subcutis, skeletal muscle, bone).
- Site: lower (55%), upper limbs (20%), trunk (20%), head/neck (5%)
- Multicentric (50%), frequent multiple nodules in the same region.
- Uncommon regional mets.
- Treatment: Surgery. Post-operative radiation therapy/adjuvant CT in few patients. MTOR inhibitors in multifocal tumors CT resistant tumors.

- Molecular Alterations: up-regulation of $FOSB$ by
  - $t(7;19)(q22;q13)$ transcript $SERPINE1-FOSB$
  - $t(7;19)(p22;q13)$ transcript $ACTB-FOSB$ (50%)
  - $WWTR1-FOSB$ (1 case)*

Pseudomyogenic hemangioendothelioma (PHE)

Infiltrative borders. Sheets, nodules, fascicles of epithelioid to spindled cells
Absent vasoformative growth pattern, Vesicular nuclei, variable nucleoli, eosinophilic, dense cytoplasm. Admixed neutrophils.
Pseudomyogenic Haemangioendothelioma

Immunoprofile

Positive Markers
- vimentin
- cytokeratin (AE1/3)
- vascular markers (ERG, FLI-1), CD31 in 50-80%
- FOSB
- SMA possible +ve stain

Negative Markers
- Desmin
- Myogenin
- CD34
- S-100
- EMA
INI1- preserved
Primary multifocal bone PMHE (boy, 3yr)

UPMC-Children’s Hospital Pittsburgh, courtesy of dr M. Reyes-Mugica/R. Sarangarajan
Primary multifocal bone PMHE (boy,3yr)
Bone-PMHE: Positive SATB2- a potential pitfall
Epithelioid hemangioendothelioma

- **Age:** all, rare in children
- **Sites with a specialized organotypic vasculature:** Deep soft tissue of extremities, viscera (most frequent in adults), bone
Epithelioid cells arranged in cords and aggregates lacking well-formed vasoformative properties.
Numerous single cells in a myxo-chondroid or sclerotic stroma
Epithelioid hemangioendothelioma

Prognostic parameters
>3cm
Mitotic rate >3/50HPF

Immunophenotype
Vascular markers: CD31, CD34, Fli1 ker-, occasionally + CAMTA1

Molecular Findings
- WWTR1-CAMTA1
- YAP1-TFE3 rearrangement*
  - Soft tissue
  - 2 cases reported in liver **
  - Histology showing voluminous eosinophilic cytoplasm with mild to moderate cytologic atypia and well-formed vascular channels
  - More aggressive clinical course, with late distant mets

*Antonescu et al. Genes, Chromosomes and Cancer, vol. 52, no. 8, pp. 775–784, 2013
Epithelioid hemangioendothelioma

Genetic Findings

Low overall mutational burden*.

- 78% of mutations in genes involved in DNA repair, epigenetic regulation, signaling pathways and cell cycle control.
- five genes potentially targetable (KMT2A, SMARCA4, BAP1, MTOR and NOTCH1)
- mutation in α-thalassemia/mental retardation syndrome X-linked gene (ATRX), recently described in EHE (more frequently found in hepatic angiosarcoma)

MIMICS OF VASCULAR LESIONS WITH EPITHELIOD CYTOLOGY
Differential diagnosis: Epithelioid Sarcoma

- Intermixed inflammatory cells
- Angiomatoid pattern (2/20 in Italian series)
- CD34+ (50%)
- Occasional expression of CD31
- INI loss, EMA+, CK+
ANGIOSARCOMA
Angiosarcoma

1-% of vascular neoplasms in children
Cases reported also in infants, some GLUT-1 positive

Other pre-existing clinical settings: congenital hemangioma, neurofibromatosis type 1, chemical exposures, chronic inflammatory processes, bilateral retinoblastoma.
Angiosarcoma in Children
Review of 5 Series * (44 cases)**

<table>
<thead>
<tr>
<th>Male: female ratio</th>
<th>0.9</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at diagnosis</td>
<td></td>
</tr>
<tr>
<td>First year of life</td>
<td>6 cases (14%)</td>
</tr>
<tr>
<td>First decade</td>
<td>18 cases (41%)</td>
</tr>
<tr>
<td>Second decade</td>
<td>26 cases (59%)</td>
</tr>
<tr>
<td>Site</td>
<td></td>
</tr>
<tr>
<td>Trunk</td>
<td>20 cases</td>
</tr>
<tr>
<td>Extremities</td>
<td>11 cases</td>
</tr>
<tr>
<td>Head and neck</td>
<td>7 cases</td>
</tr>
<tr>
<td>Viscera **</td>
<td>6 cases</td>
</tr>
<tr>
<td>Dead of disease:</td>
<td>25 cases (57%)</td>
</tr>
</tbody>
</table>

**Visceral sites included liver (3 cases), spleen (1 case), both liver and spleen (1 case), and heart (1 case).
**AS:** anastomosing vessels lined by a single layer of endothelial cells with moderate atypia. Highly infiltrative growth pattern, epithelioid cells prominent.
AS, maxillary region M, 17y DOD (1 yr): poorly-differentiated areas with pleomorphism, mitotic activity, inconspicuous lumina
Immunophenotype

- CD31,
- CD34,
- von Willebrand factor
- VEGFR-3
- ERG+
- D2-40 variable
- HHV8 –
Visceral AS, with spindle cell morphology
12 yr, F Vaginal bleeding
Main Mass

Nodules in the bowel wall
Immunohistochemical profile

Positive
- CD117
- CD34
- **CD31**
- ERG
- FVIII

INI preserved

Negative
- MNF-116
- SMA
- Desm
- Myf4
- S100
- MSA
- EMA
- ER,PR
- CD10
Pediatric Angiosarcoma: What about genetic features?

PLCG1, KDR mutations MYC gene amplifications
FLT4 amplifications in Adult AS, mostly post-radiation therapy

CIC abnormalities in 9% (9/98): 6 CIC mutated, 3 CIC-rearranged AS
Younger patients with primary AS
Inferior disease-free survival
CIC-rearranged AS: no vasoformation, solid growth of round, epithelioid to rhabdoid cells,
Transcriptional signature like other round cell sarcomas, included CIC-rearranged tumors.

Hepatic Angiosarcoma (Former Type 2 HE, Dehner)

5yr chinese girl
History of hepatic hemangioma at birth
(Hemangioendothelioma type 1) at birth
Treatment with propanolol
Now a huge hepatic mass rapidly growing
Immunophenotype

ER
G

CD31
At autopsy

Other organs free from mets

Is OLT an option in these patients?

The term “angiosarcoma” excludes the patient from transplant
Widening Spectrum of Liver Angiosarcoma in Children

*Oanez Ackermann, †Monique Fabre, ‡Stephanie Franchi, §Daniele Pariente, Dominique Debray, Emmanuel Jacquemin, Frederic Gauthier, and Olivier Bernard

ABSTRACT

Objectives: Liver hemangiomas are vascular tumors, which occur in the first months of life and carry risks of initial complications, but are considered to be benign histologically and to regress with time. Histologic studies suggest that a subtype, type 2 hemangioendothelioma, is akin to angiosarcoma and may have a severe long-term prognosis. We report 5 girls with type 2 hemangioendothelioma of the liver.

Methods and Results: Three children initially presented with classical infantile multinodular hemangioma, including cardiac and pulmonary complications and regression of tumors at age 1½ to 2½ years. All 3 experienced tumor relapse at ages 2½ to 3, leading to death at ages 2½ to 5. Tumor histology showed type 2 hemangioendothelioma. The other 2 children presented with liver tumors at ages 2 and 3 years. In 1, initial biopsy of a single tumor showed benign type 1 hemangioendothelioma, but surgical resection was followed by relapse in the remaining liver, lung metastases, and death. Whole tumor histology showed both type 1 and 2 lesions. In the other child, tumor biopsy showed type 2 lesions. She underwent liver transplantation and is alive without tumor recurrence 3 years later.

Conclusions: Careful follow-up is necessary to detect late recurrence in infants with multinodular liver hemangiomas. Vascular liver tumors occurring after infancy are likely to be malignant. The high risk of relapse in the remaining liver suggests that if no metastases are detected, liver transplantation is preferable to surgical tumor resection in both situations.

Key Words: infantile hepatic hemangioma, liver angiosarcoma, liver transplantation, vascular liver tumor

(JPGN 2011;53: 615–619)
How will we treat these children?

“Angiosarcoma, that is, HE type 2, in children still is considered an uncontrollable oncological problem. Nonetheless, if localized in the pediatric liver and not associated with metastasis, LT may be a way out, with a good prognosis.

In contrast, in adults, the results of LT for angiosarcoma are disastrous and angiosarcoma remains an absolute contraindication to LT.
CONCLUSIONS
“Borderline” and malignant vascular tumors in children are rarities

A subset is typical of childhood and a systematic clinico-pathologic approach is needed to achieve a correct diagnosis

Adult-type vascular tumors (such as AS) are probably biologically different entities, histologically challenging and need a wide immunohistochemical panel: often represent an unexpected diagnosis

Lymphatic lesions require a complete immunohistochemical panel being the different markers (D2-40, VEGF3, LYVE, PROX1) irreguarly expressed
John Baldessari
American, b. 1931

Cigar Dreams (Seeing Is Believing), October 1974
From the series Embed
Gelatin silver prints

The smoke airbrushed onto these three images spells the words (from left to right) Seeing / is / believing. Baldessari created this triptych shortly after the publication of Wilson Bryan Key’s Subliminal Seduction, a bestseller that warned of the influence of hidden words and symbols in advertising photography. Baldessari’s concealed message floats over the repeated image of a cigar in an ashtray—perhaps in reference to the remark apocryphally attributed to Sigmund Freud: “Sometimes a cigar is just a cigar.”