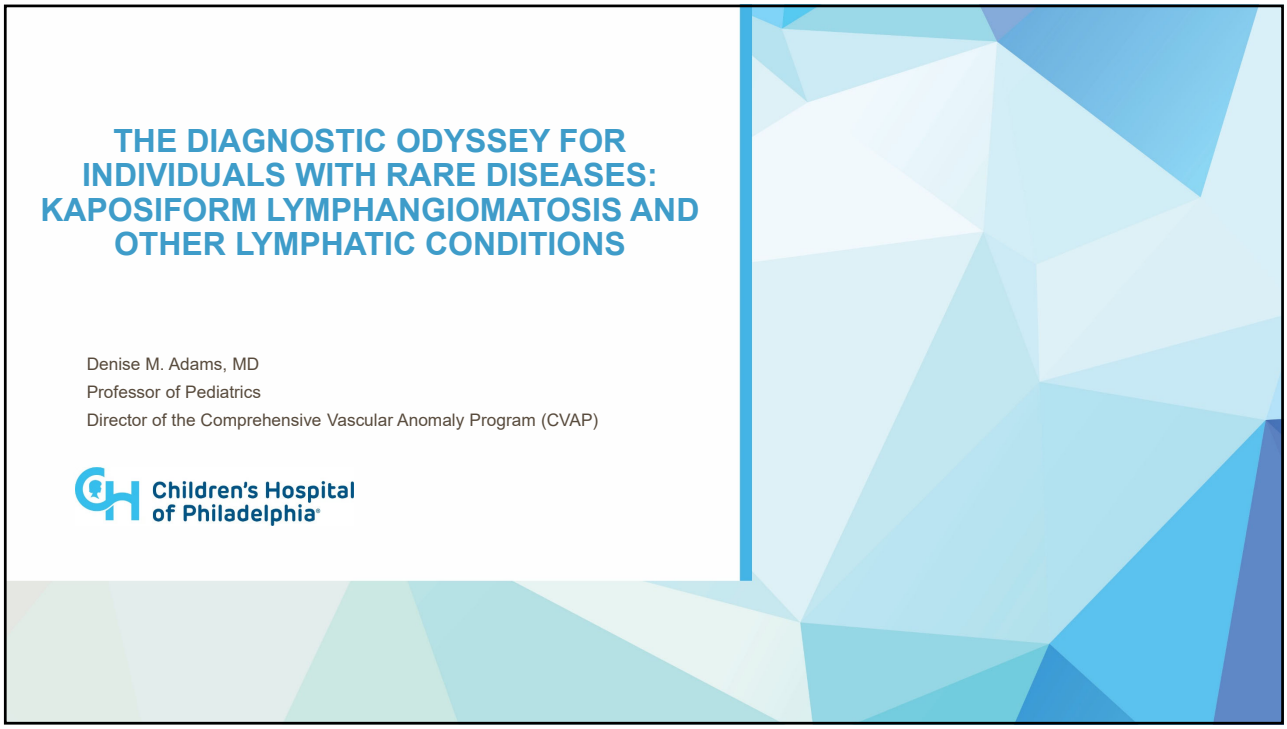

1

LEARNING OBJECTIVES

At the end of this educational activity, participants should be able to:

- Describe the diagnostic journey for individuals with kaposiform lymphangiomatosis (KLA) and other lymphatic conditions.
- Explain emerging diagnostic tools and therapies, including clinical trials for KLA and other lymphatic conditions.
- Discuss challenges and barriers in the diagnosis and treatment of KLA as well as the associated physical and mental health issues.
- Incorporate individual and caregiver engagement in shared decision-making.
- Summarize interprofessional team strategies for improving coordination and communication to support the well-being of both the individual and their family/caregiver(s).

2

OUTLINE

- Comprehensive Vascular Anomalies Program (CVAP)
- Classification of Vascular Anomalies
- A Patient Story
- Complicated Lymphatic Anomalies
- Lessons Learned: The Power of One
- Genotype/Phenotype Discoveries
- Collaboration

3

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COMPREHENSIVE VASCULAR ANOMALIES PROGRAM (CVAP) TEAM

Denise Adams, MD Hematologist/Oncologist **Director of CVAP, Co-Director of CVA Frontier Program**

Hakon Hakonarson, MD, PhD Director of Center for Applied Genomics (CAG); **Co-Director of CVA Frontier Program**

Lauren N Sewter MSN, RN, CRNP Sr Manager Clinical Program Operations

Anne Marie Cahill, MBBch, BAO Division Chief, IR & **Director of Image Based Therapy for VA**

Abhay "Finn" Srinivasan, MD Diagnostic & Interventional Radiologist

Alexandra Borst, MD Hematologist/ Oncologist

Seth Vatshky, DO Interventional Radiologist

David Low, MD Plastic Surgeon

Joe Napoli MD, DDS Plastic Surgeon

Jim Treat, MD Dermatologist

Yoav Dori, MD, PhD Director Jill and Mark Fishman Center for LA

Christopher Smith, MD, PhD Cardiologist

Connor Devine, MD Otolaryngologist

Alexandre Arkader, MD Orthopedic Surgeon

David Weber, MD, MSCE Endocrinologist

Jefferson N. Brownell, MD, MS Gastroenterologist

William Rocamora Katowitz, MD Ophthalmologist

Lauren Beslow, MD Pediatric Neurologist

Lea Surrey, MD, Pathologist, Director, Division of Genomic Diagnostics

Ryan DeLeo, MS OTR/L Occupational Therapist

Elizabeth Cross, PT, DPT, MSW, CLT Physical Therapist

Shivangi Argade, MSN, CRNP-AC/PC, RN

Dong Li, PhD, Research Scientist, Center for Applied Genomics

Asia Sibert-el Complex Scheduler

Pablo Laje (General Surgery)

Dionne Haskins Access Coordinator

Tressa Hobart Admin Program Coordinator

Marguerite Weisman, RN Nurse Navigator

Stephanie Adams, RN Nurse Navigator

Melissa Casey, BS, MB Administrative Manager Clinical Research

Tamjeed Sikder, MS Clinical Research Coordinator

Marla Dimercurio LCSW, Clinical Research Coordinator

Lydia Williams, Clinical Research Assistant

Abaigeal Doherty, LSW Medical Social Worker

Allison Britt, MS, LCGC Genetic Counselor

4

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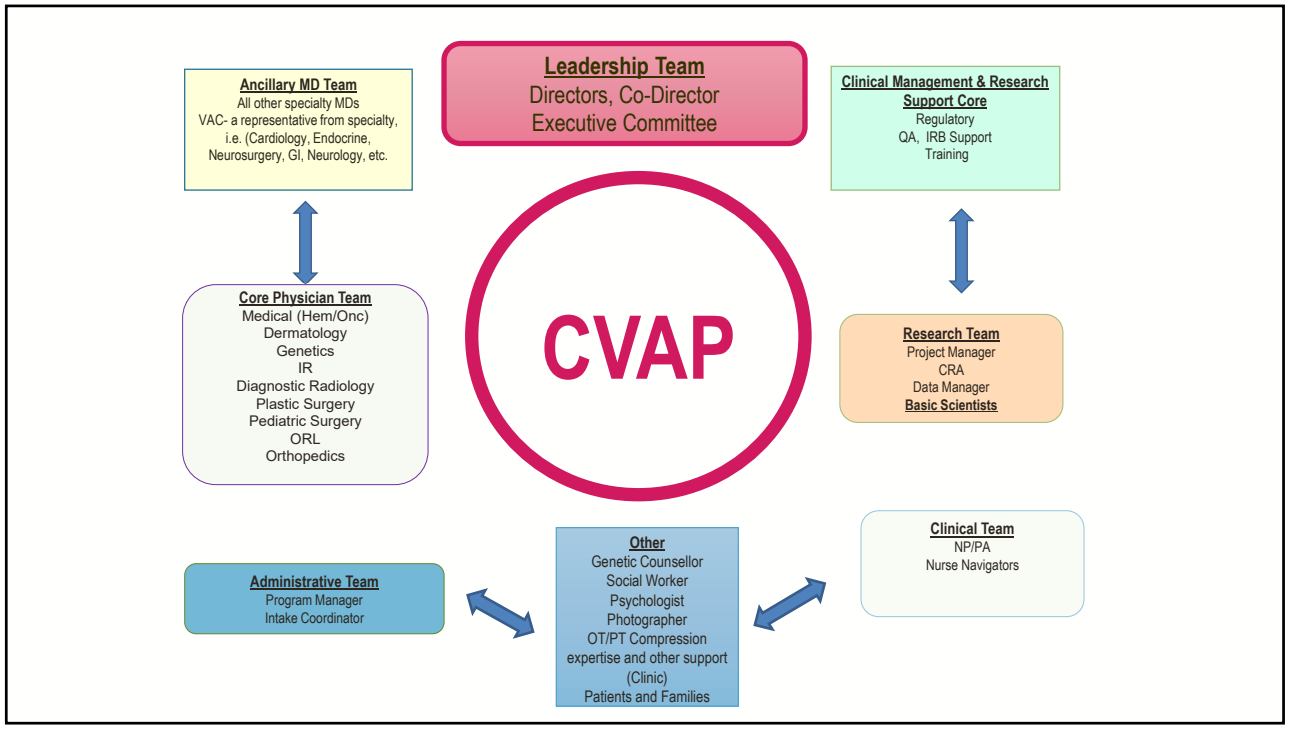
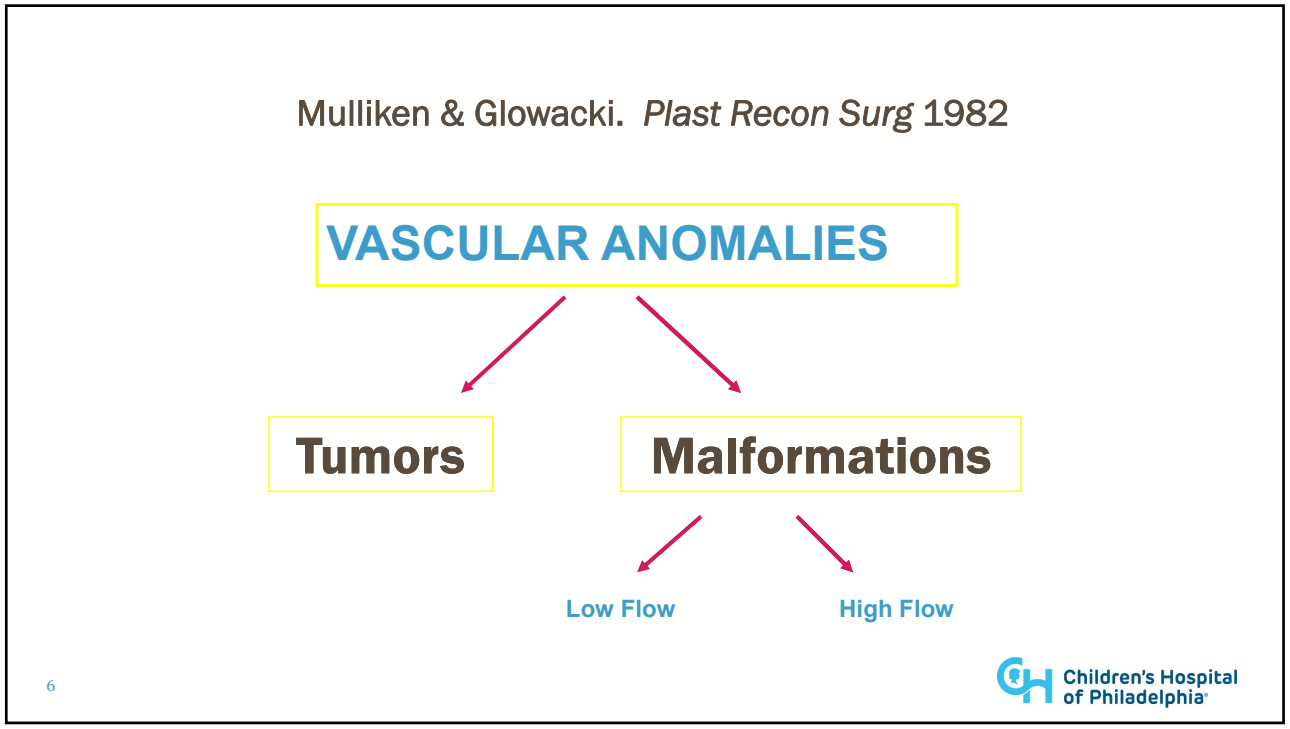
4


Ancillary MD Team
All other specialty MDs
VAC- a representative from specialty, i.e. (Cardiology, Endocrine, Neurosurgery, GI, Neurology, etc.
Leadership Team
Directors, Co-Director
Executive Committee
Clinical Management & Research Support Core
Regulatory
QA, IRB Support
Training
CVAP
Core Physician Team
Medical (Hem/Onc)
Dermatology
Genetics
IR
Diagnostic Radiology
Plastic Surgery
Pediatric Surgery
ORL
Orthopedics
Research Team
Project Manager
CRA
Data Manager
Basic Scientists
Other
Genetic Counsellor
Social Worker
Psychologist
Photographer
OT/PT Compression expertise and other support (Clinic)
Patients and Families
Clinical Team
NP/PA
Nurse Navigators
Administrative Team
Program Manager
Intake Coordinator

5


Mulliken & Glowacki. Plast Recon Surg 1982
VASCULAR ANOMALIES
Tumors
Malformations
Low Flow
High Flow
6
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6

ISSVA CLASSIFICATION – 2014, 2018,2022

(WASSAF ET AL *PEDIATRICS* VOL 136 NUMBER 1, JULY 2015)

ISSVA classification for vascular anomalies
(Approved at the 20th ISSVA Workshop, Melbourne, April 2014)

Overview table

Vascular anomalies				
Vascular tumors	Vascular malformations			
	Simple	Combined *	of major named vessels	associated with other anomalies
Benign Locally aggressive or borderline Malignant	Capillary malformations Lymphatic malformations Venous malformations Arteriovenous malformations* Arteriovenous fistula*	CVM, CLM LVM, CLVM CAVM* CLAVM* others	See details	See list

* defined as two or more vascular malformations found in one lesion
* high-flow lesions

N.B. The classification tables do not list exhaustively all known vascular anomalies.
Some rare "dermatologic" vascular anomalies will be found in dermatology textbooks.

The tumor or malformation nature or precise classification of some lesions is still unclear.
These lesions appear in a separate provisional list.

Abbreviations used

For more details, click on the underlined links

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IMPROVED CLASSIFICATION

- New Diagnoses
- Anatomical Variants
- Named Syndromes
- Known and Accepted Genetic Causes

- **Recently updated in 2018 in Amsterdam**

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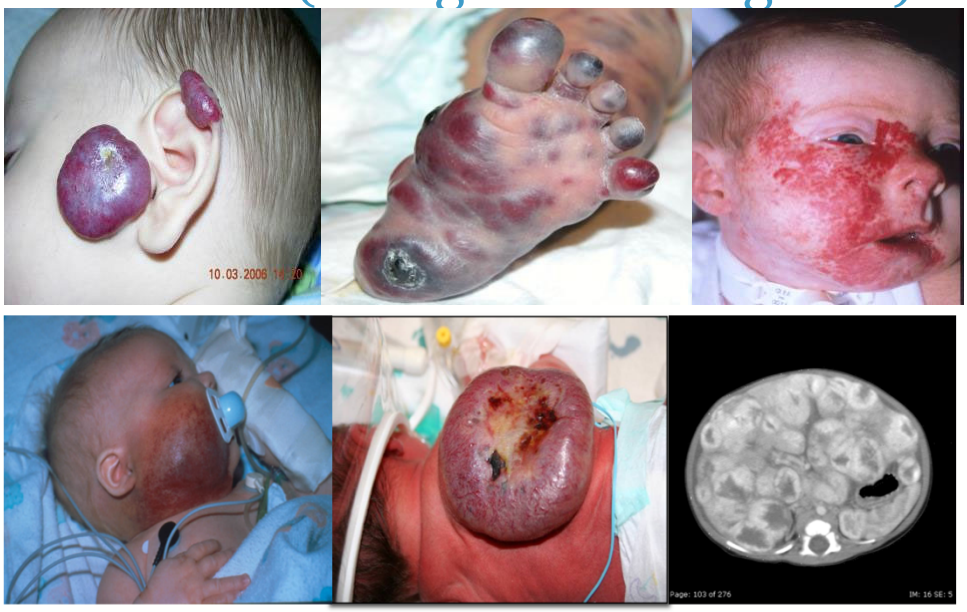
Tumors (Benign and Malignant)



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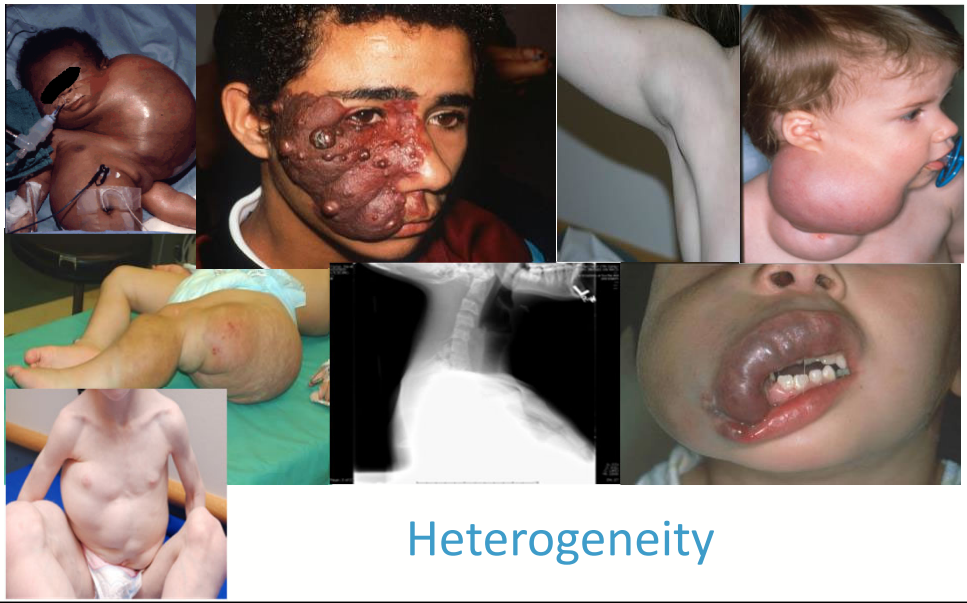
VASCULAR MALFORMATIONS



Heterogeneity

10

OUR PROBLEM

What the MD contemplates

Phenotype:

- History
- Clinical Exam
- Radiology
- Pathology

Genotype:

- Somatic
- Germline

Why is this difficult

- Rare diagnoses do not fit into a perfect box
- Expertise is not found everywhere
- Lack of training in medical school, nursing school and other allied health professions
- Delay in diagnosis
- Many interventions as there is no standard of practice
- Anxious patients and families searching for answers leading to more stress and anxiety

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LYMPHATIC ANOMALIES

12

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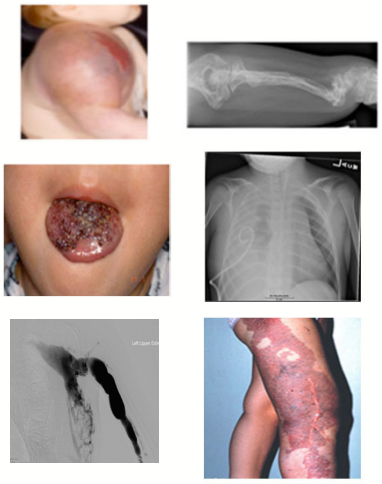
COMPLICATIONS



- Bleeding and infections
- Bone and soft tissue involvement: pain, swelling
- Lymphatic blebs: leakage, bleeding, anemia
- Effusions: respiratory distress, chronic lung disease
- Dilated veins: phlebitis, risk of thrombosis
- Overgrowth: functional issues, pain, orthopedic issues
- Coagulopathy

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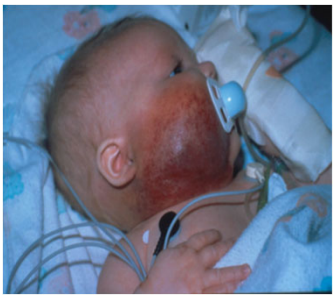
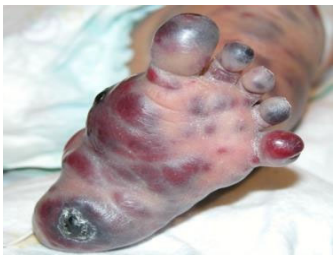
LYMPHATIC TUMORS

- Kaposiform Hemangioendothelioma (KHE)
  - Intermediate malignancy
  - No metastatic potential



- Lymphangiosarcoma
  - Malignant



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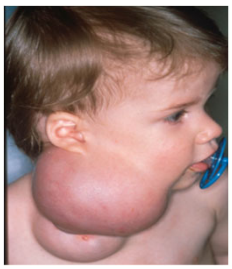
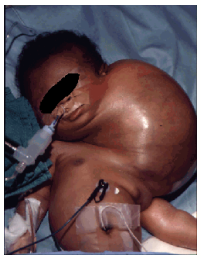
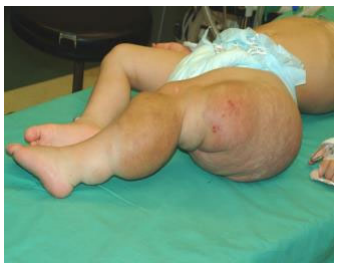
LYMPHATIC MALFORMATIONS



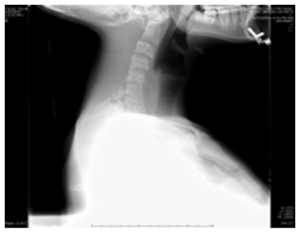
Macrocystic LM



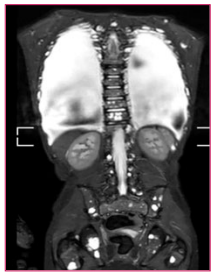
Microcystic LM



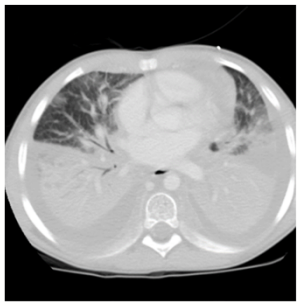
Combined VM(CLVM)



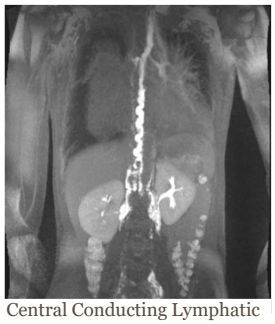
Gorham Stout Disease (GSD)



Generalized Lymphatic Anomaly (GLA)



Kaposiform Lymphangiomatosis (KLA)



Central Conducting Lymphatic Anomaly (CCLA)

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15

A PATIENT STORY

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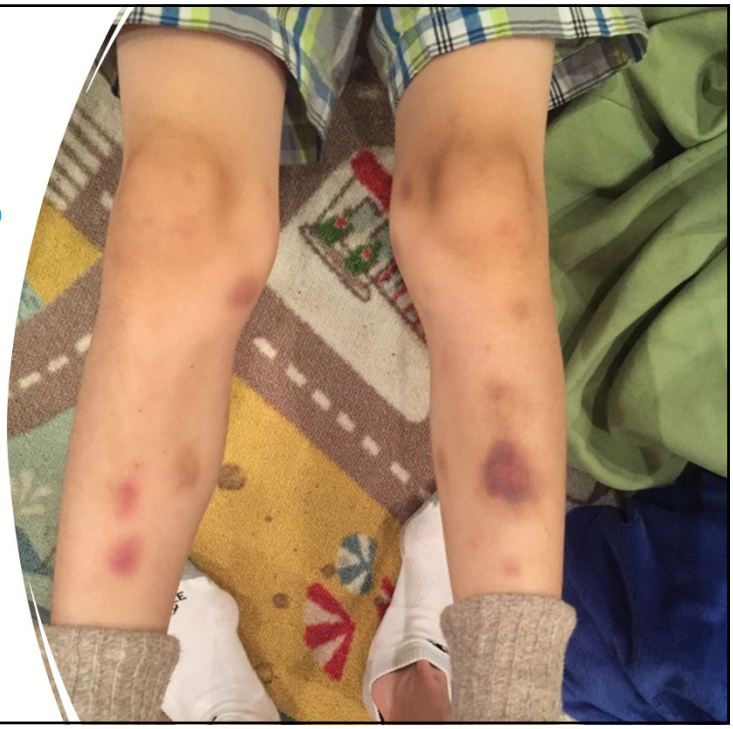
MICHAEL ALEXANDER PROKOPOWICZ

- Born on May 13, 2009
- 8 lbs. 5 oz.
- Happy and healthy and super smart

17

CONCERNING SYMPTOMS STARTED AT AGE 5

- Fever
- Rash
- Bone pain
- Unexplained swelling in groin and scrotum
- Poor appetite
- Fatigue
- Unusual bruising



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LOOKING FOR AN EXPLANATION: CONSULTATION WITH SPECIALISTS

- Hematology
- Urology
- Orthopedics
- Endocrinology
- Rheumatology
- Neurology
- GI
- Pulmonary
- Cardiology
- Nutrition
- Physical Therapy
- Occupational Therapy

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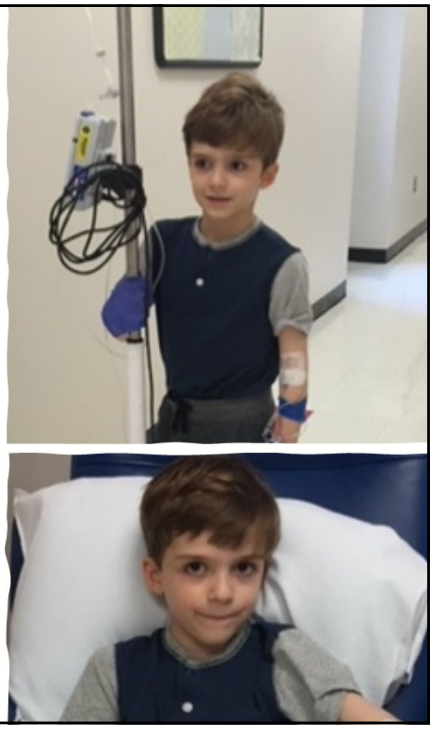
MANY SCARY DIAGNOSES CONSIDERED OVER 12 MONTHS

- Parvovirus
- ITP
- Hydrocele
- Inguinal hernia
- Viral epididymitis
- Behavioral anorexia
- CMV, EBV, ehrlichiosis, Lyme, brucellosis
- Systemic lupus
- Cystic fibrosis
- Fanconi's anemia
- Dyskeratosis congenita
- PNH
- Aplastic anemia
- Von Willebrand's



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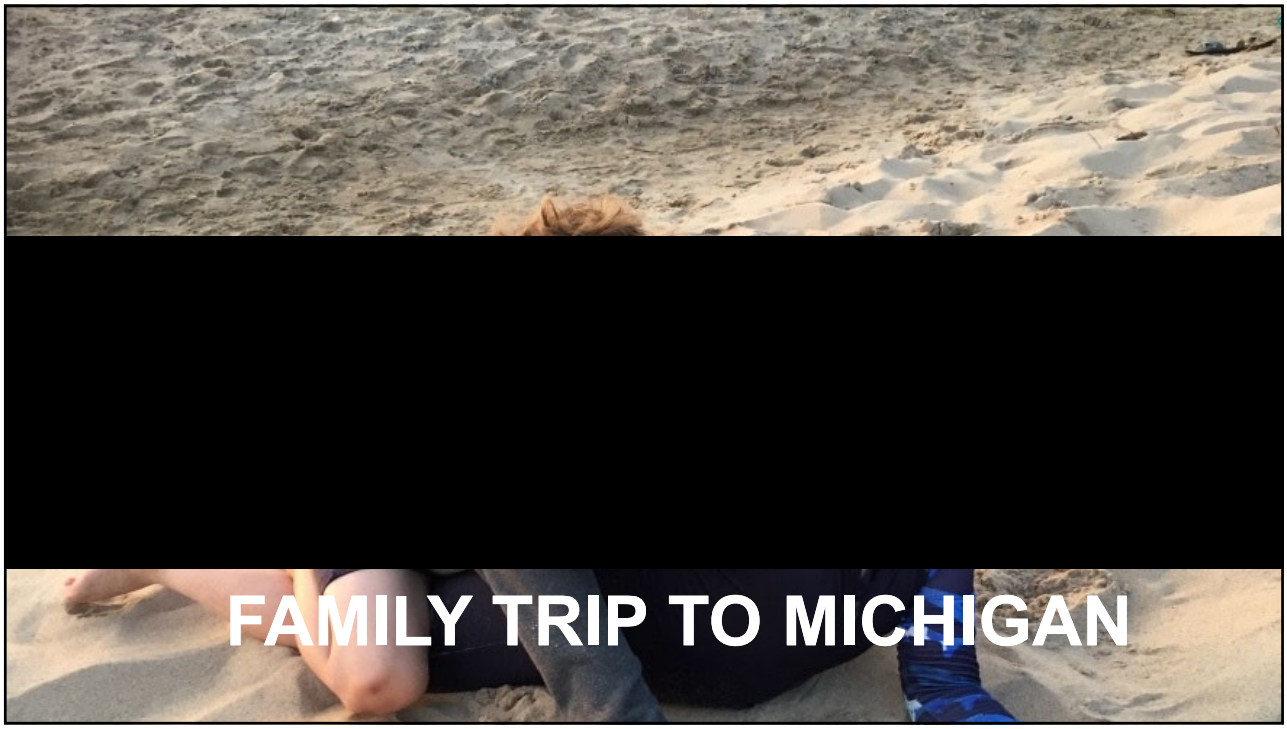

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A MINOR BUMP ON THE HEAD TAKES A SERIOUS TURN

- "Goose egg" on the head rapidly expands to diffuse scalp swelling
- Seen urgently by local hematologist
- Platelets and fibrinogen low
- Pain and swelling worsened
- Drove to ER at University of Michigan

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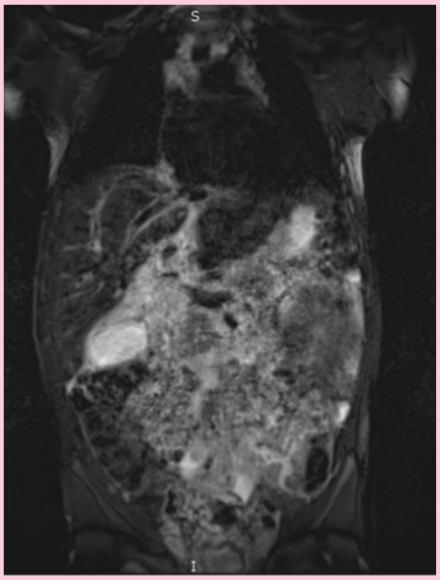
UNEXPECTED DIAGNOSIS: DIFFUSE LYMPHANGIOMATOSIS

- MRI report read when we arrived back in Baltimore
- Didn't know what diagnosis meant: turned to Google
  - *"Diffuse lymphangiomatosis has a poor prognosis and no cure. It is characterized by slow progressive growth of lymphatics commonly with chylous effusions and may be associated with lytic bone lesions and mediastinal compression."*
- Looked online for anyone we thought might help and sent many emails



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REACHED OUT

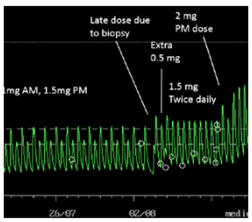
- Recommended a biopsy to confirm diagnosis

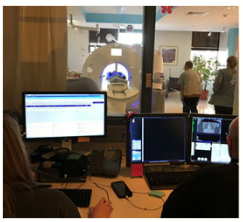
- Started on sirolimus (troughs, PK studies if needed)

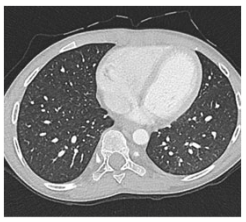
- **Words of wisdom**: "Do not read about this" & "Take care of yourself and your marriage"

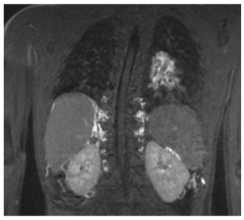
- Discussed other specialists that we will need (pulmonary, IR, cardiology, endocrine, ortho)

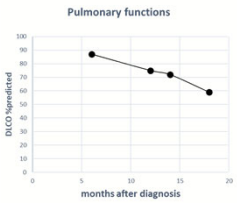
- I asked about what research was being done and how I can help











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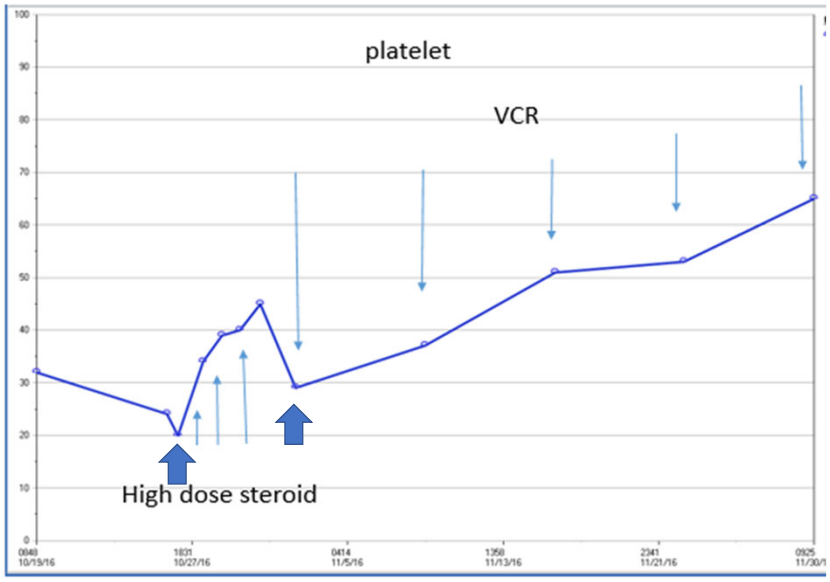
A YEAR OF CHEMOTHERAPY



- Unable to lower steroids despite use of sirolimus
- Decided to add IV vincristine
- Usually requires placement of a port
- Convinced team to try giving it through IV

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Lymphatic Education & Research Network

LGDA

RESEARCHERS AND CLINICIANS WORLDWIDE

- Denise Adams MD, CHOP
- Steve Fishman, MD, Meghan O'hare, NP Boston Children's
- Philip John, MD (Sick Kids)
- Samira Syed MD, GOSH
- Matt Warman MD Boston Children's (tissue for sequencing)
- Tim LeCras PhD, CCH (serum markers, angiopoietin-2) Cincinnati Children's
- Max Itkin MD, UPenn
- Yoav Dori MD PhD, CHOP
- Hakon Hakonarson MD PhD, Sarah Sheppard MD, CHOP
- Stan Rockson, MD, Stanford
- Janet Crane, MD, Hopkins
- Cliff Takemoto, MD, St. Jude's
- Michael Dellinger PhD, UT Southwestern
- Christopher Towe MD, CCH
- Sequencing by Illumina and GeneDx
- Yaser Diab MD, Children's National
- Francis Collins MD PhD, and Zorina Galis, PhD., PJ Brooks, PhD, NIH
- LE&RN, (Bill, Phyllis)
- Lymphangiomatosis Gorham's Disease Association Registry (LGDA)

27

POTENTIAL IMPACT OF A SINGLE CASE REPORT

Pediatric Blood & Cancer

HEMATOLOGY: BRIEF REPORT | Free Access

Kaposiform lymphangiomatosis treated with multimodal therapy improves coagulopathy and reduces blood angiopoietin-2 levels

Janet Crane, Jackie Manfredo, Elisa Boscolo, Mara Coyan, Clifford Takemoto, Maxim Itkin, Denise M. Adams, Timothy D. Le Cras

First published: 07 July 2020 | https://doi.org/10.1002/pbc.28529

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September 2020
e28529

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LESSONS LEARNED

- Diagnosis can be difficult even for those with a medical background
- Social media can bring vital information to patients with rare diseases and their families
- Clinicians and researchers can benefit from the patient community
- Imagine how this is for those with no medical knowledge who are not close to a major medical center…

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LYMPHATIC MALFORMATIONS

- Macrocystic vs. microcystic
- Head and neck most common location
- Swelling, pain, infection, disfigurement, bone involvement
- Isolated LMs frequently with mutations in *PIK3CA*

- Diagnosis – US, PE, MRI, but CT may be helpful for bony lesions
  → consider possibility of pleural/pericardial effusions and bony vertebral lesions, avoid biopsy

- Treatment – sclerotherapy, full vs partial resection, sirolimus, antibiotics/steroids if infected, compression
- PIK3CA mutations

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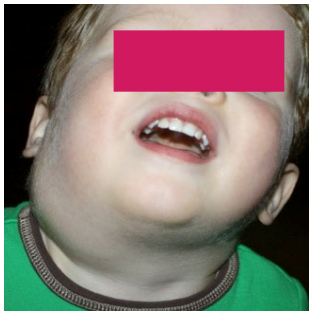
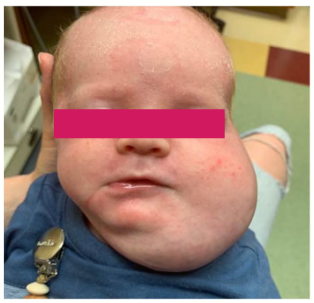
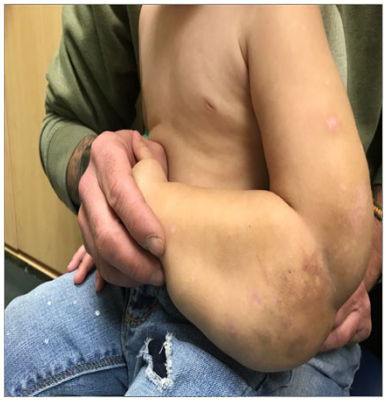
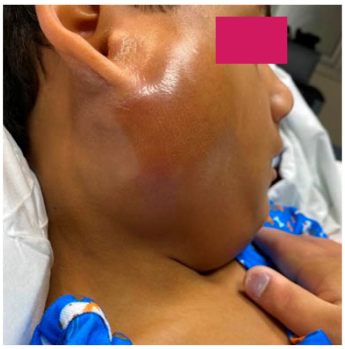

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GENERALIZED LYMPHATIC ANOMALY (GLA)

- Previously known as lymphangiomatosis
- Non-neoplastic, multicentric proliferation of dilated lymphatic vessels, resembling a common LM
- Likely present since birth but becomes clinically significant usually within first 2 decades of life
- Affects bone, liver, spleen, mediastinum, lung, and soft tissues
- Bone involvement is osteolytic (punched out lesions, cortex intact)
- Clinical response depends on location and extent, thoracic involvement has worst prognosis
- PIK3CA mutations

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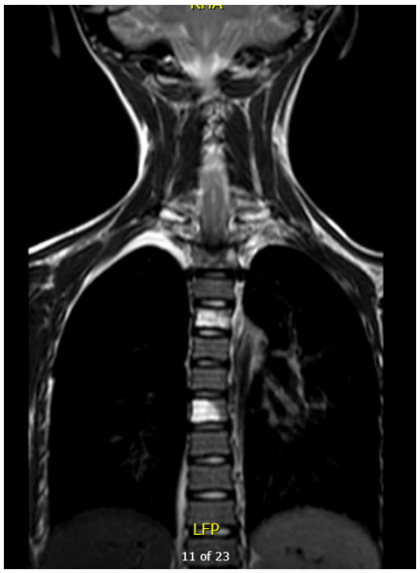

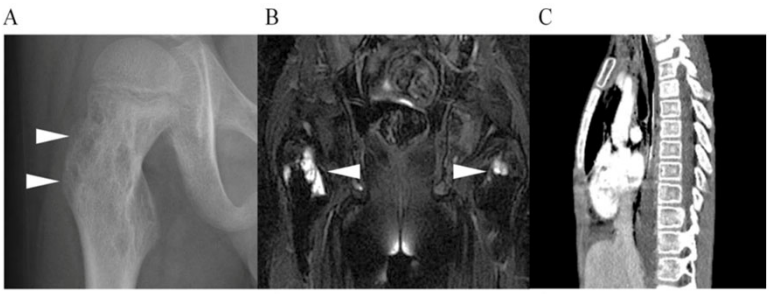

Ozeki et al. *Pediatr Blood Cancer* 2016

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GORHAM STOUT DISEASE (GSD)

- Aka *vanishing bone disease*
- Significant clinical overlap with GLA, but tends to involve single site (or adjacent sites) bone and there is osteolysis of both medullary areas and cortex
- Upper axial skeleton most commonly affected
- Often associated with adjacent soft tissue mass or areas of microcystic LM
- Osteolysis can be profound and can result in unstable situations → cervical/spinal instability or non-functional appendages
- KRAS

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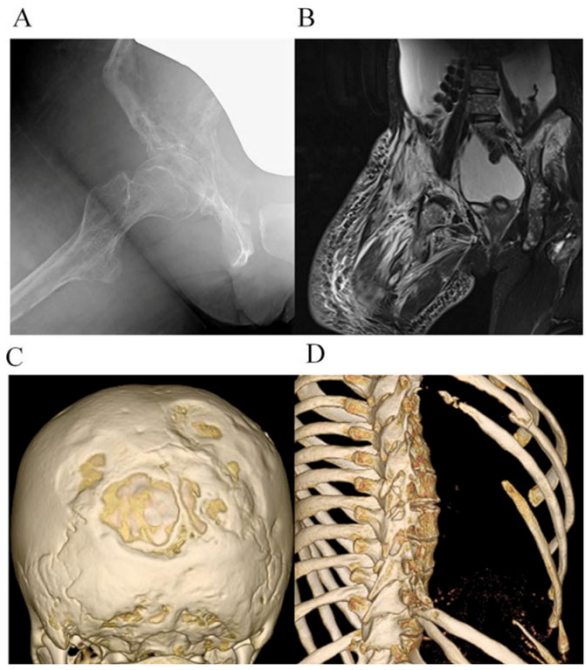

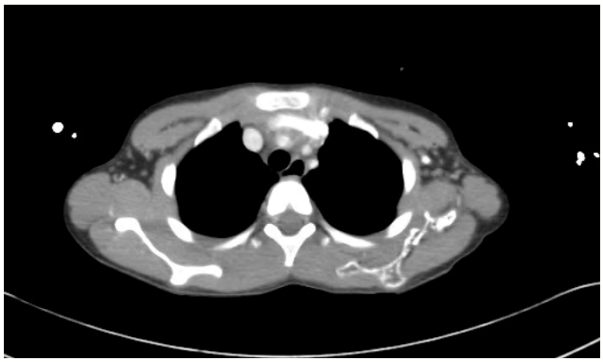

Ozeki et al. *Pediatr Blood Cancer* 2016

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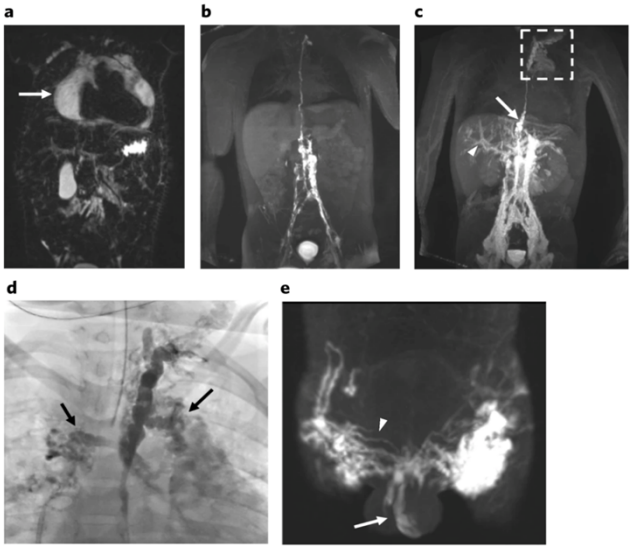
CENTRAL CONDUCTING LYMPHATIC ANOMALY (CCLA)

- Abnormal lymphatic vessels that lead to dilated vessels and cysts and reflux of lymphatic fluid/chyle into soft tissues
- Best characterized by or MR lymphangiography
- Mostly Rasopathies



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KAPOSIFORM LYMPHANGIOMATOSIS (KLA)

- Considered an aggressive subtype of GLA, but histologically distinct
  → foci of spindle endothelial cells on a background of malformed lymphatic vessels
- Usually involves multiple organs, but predominantly thoracic cavity and causes significant (life-threatening) pleural effusions
- KLA effusions more likely to be frankly hemorrhagic than GLA
- Patients often coagulopathic at presentation (elevated D-dimer, hypofibrinogenemia, thrombocytopenia)
- Usually presents at a younger age than GLA and GSD and has higher morbidity/mortality
- Mortality 50-60% historically
- NRAS, PIK3CA

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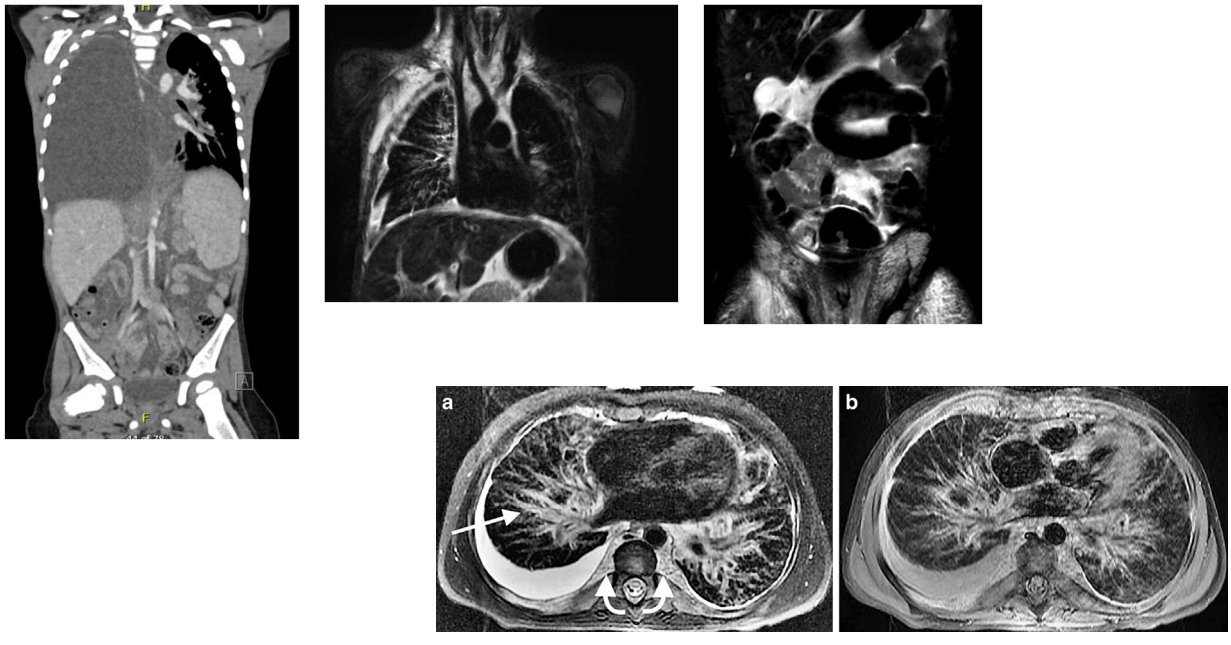

Goyal et al. *J Pediatr Radiol* 2016

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INTERVENTIONAL OPTIONS

- Sclerotherapy
- Embolization
- Lymphatic Intervention

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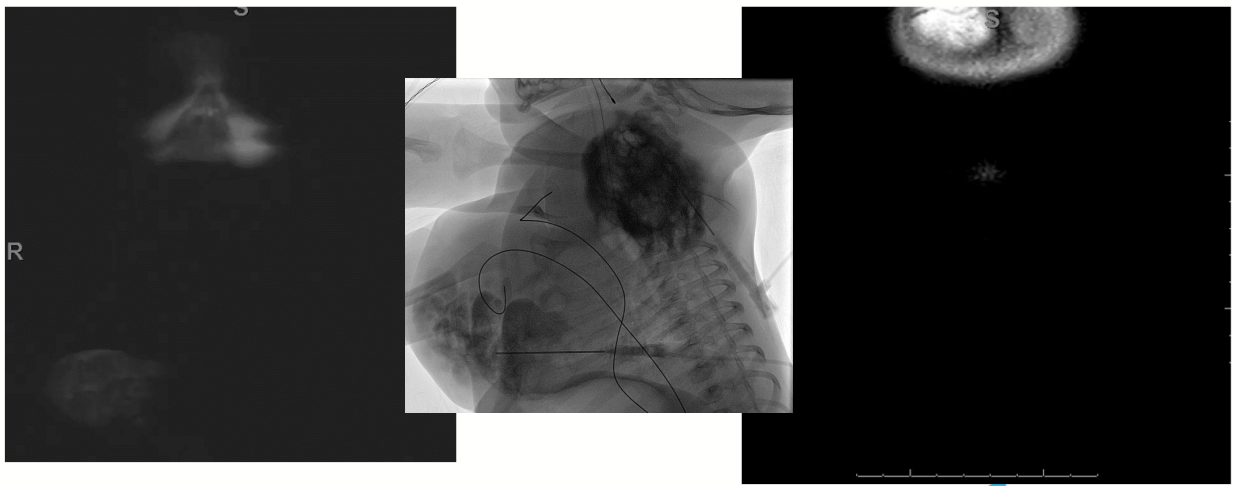
NEONATE WITH LARGE LYMPHATIC MALFORMATION



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EMBOLIZATION

- Occlusion of a vessel, performed endovascularly.
  - Glue
  - Concentrated ethanol
  - Particles (plastic beads)
  - Coils

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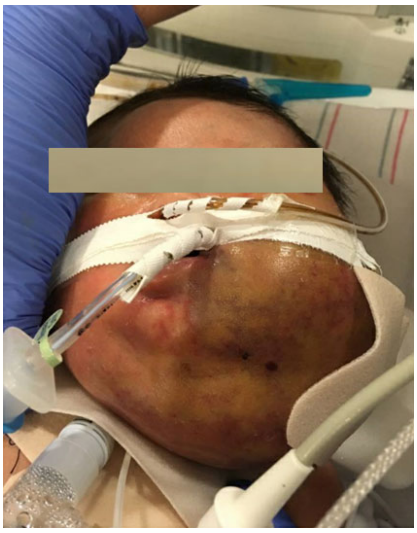
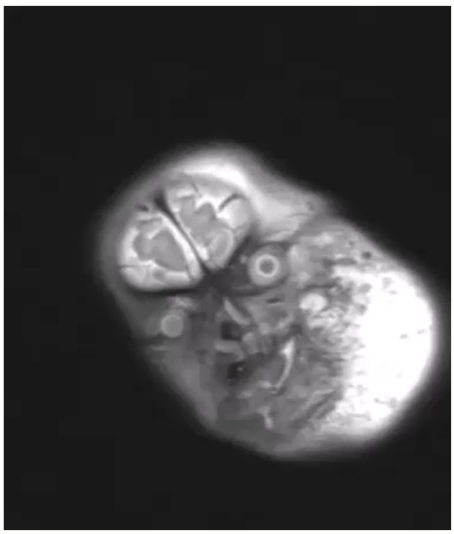
1 DAY-OLD, WITH KAPOSIFORM HEMANGIOENDOTHELIOMA, HEART FAILURE, CONSUMING PLATELETS





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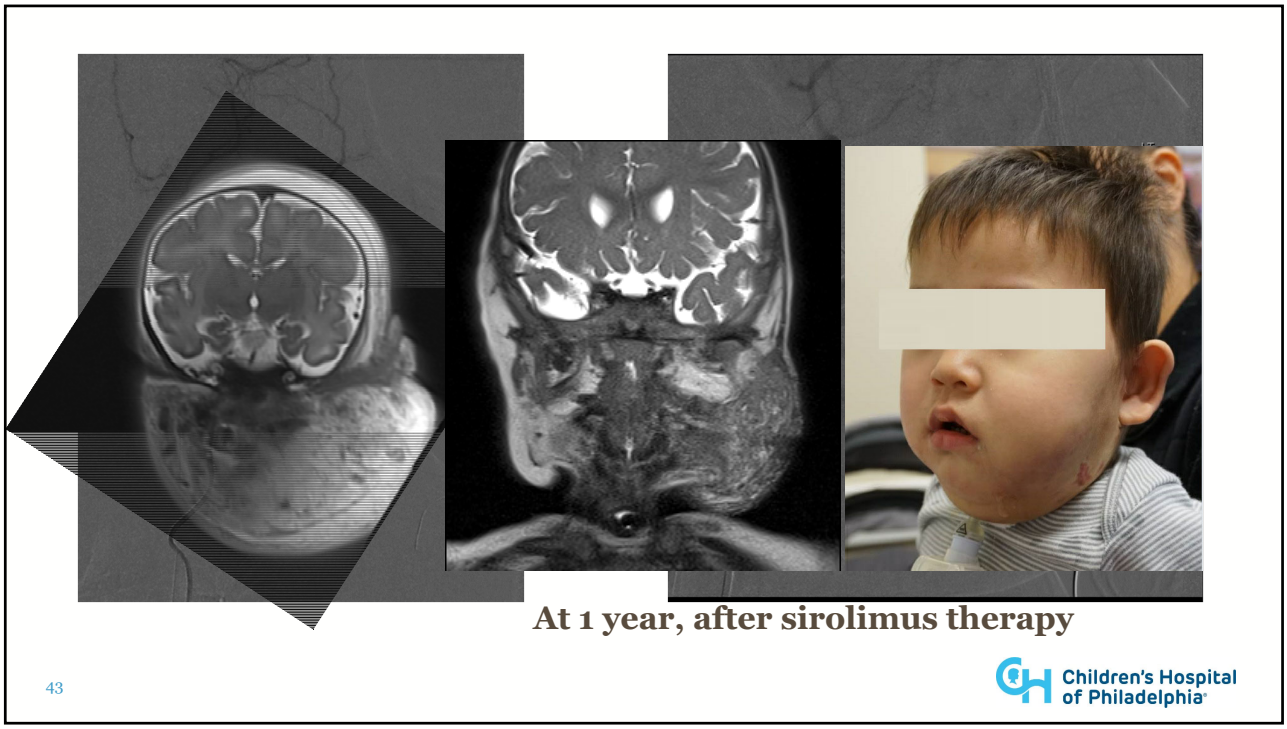

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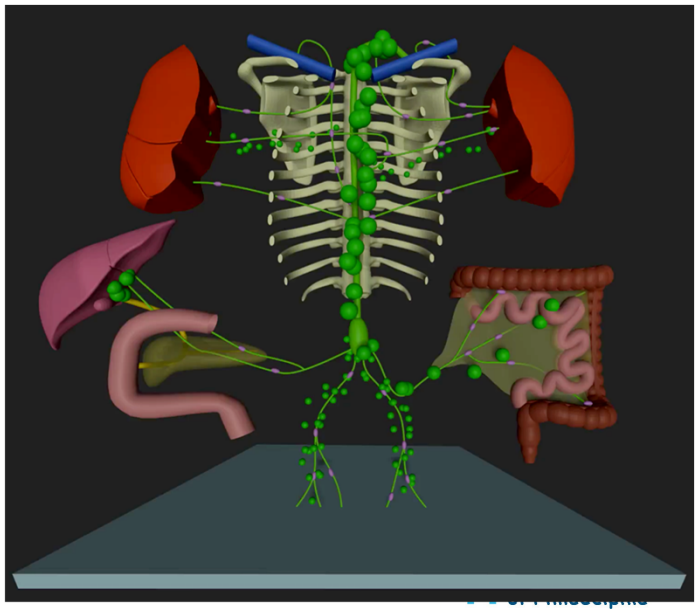
LYMPHATIC ANATOMY AND FLOW

- Lymphatic anatomy and physiology was extensively studied up to the 1970s.

40-year hiatus

- Absence of lymphatic imaging methods
- Absence of interventional techniques



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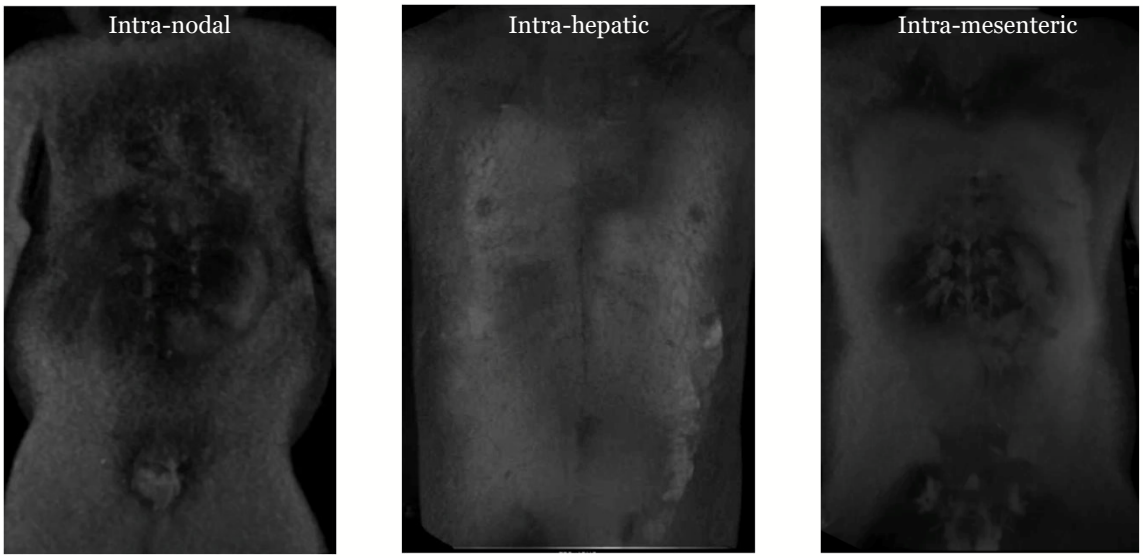
MR LYMPHANGIOGRAPHY



Biko et al. *Eur J. Rad* 2019, Dori *et al. Radiology* 2014, Dori *et al. Pediatrics* 2014, Dori *et al. Eur. Rad.* 2020, Krishnamurthy *et al. Radiology* 2015

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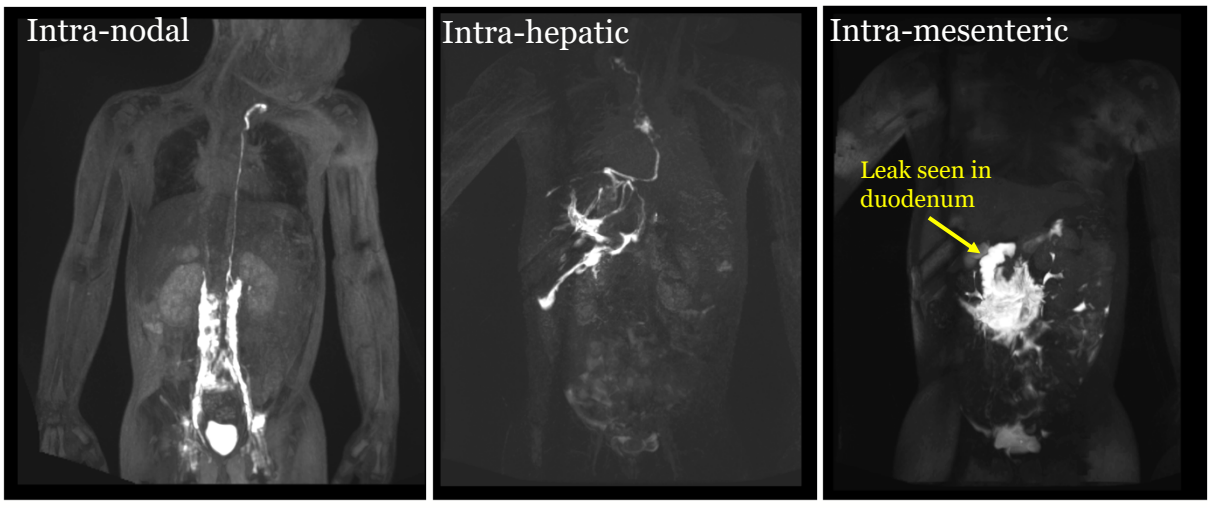
7 YEAR-OLD WITH CCLA AND CONGENITAL PLE



Dori *et al. Eur. Rad.* 2020

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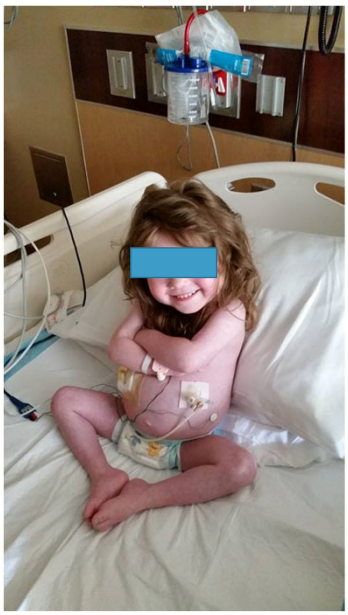
OUTCOME AFTER PLE TREATMENT



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RADIOLOGY AND VASCULAR ANOMALIES: THE FUTURE

- Continued refinement and revision of lesion classification based on advances in imaging
- Further refinement in sclerotherapy, embolization, and ablation techniques
- Local drug delivery:
  - Using techniques in sclerotherapy & embolization
  - Ultrasound-assisted drug delivery

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MEDICAL TREATMENT OPTIONS

The Power of One

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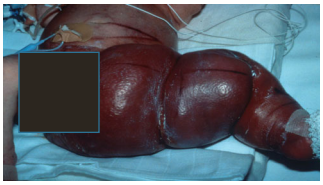
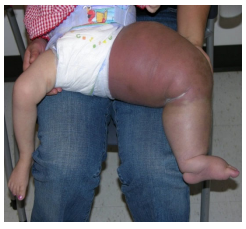
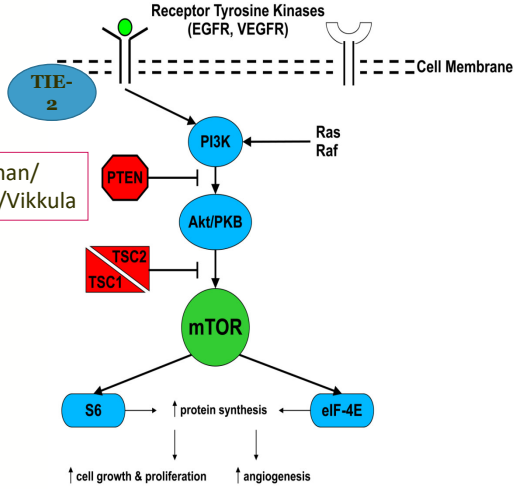
THE POWER OF ONE
HOW ONE PATIENT CHANGED OUR THINKING….. (2007)





Vincristine/Steroids
Cyclophosphamide
Amicar
Avastin
Sirolimus

Warman/
Boon/Vikkula



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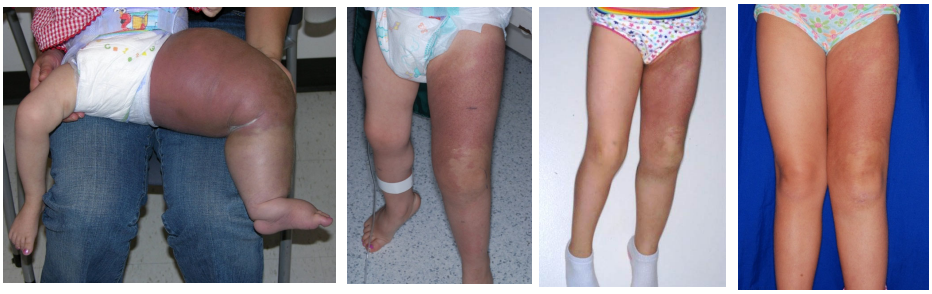
MTOR INHIBITOR - SIROLIMUS



Starting sirolimus therapy | 21 months on | 18 months off | Recent

ISSVA 2010

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MTOR INHIBITORS

- Sirolimus
- (Everolimus)
- Initially developed as an anti-fungal agent
- PK and PD well developed even in infants
- Treatment long term
- Can be used in conjunction with surgery and sclerotherapy
- Mechanism:
  - Blocks the activity of mammalian target of rapamycin
  - Protein kinase that regulates Growth factors that stimulate Cell growth, differentiation and angiogenesis
- Side Effects
  - Immunosuppression
  - Mouth Sores
  - Headaches
  - GI complaints
  - Metabolic issues
  - Anemia
  - Hyperlipidemia
  - Pneumonitis
  - Effusions
- FDA approved for transplant, LAM, TS

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SIROLIMUS AND VASCULAR ANOMALIES

Over 100 articles in PubMed

Other ongoing (Clinical Trial.gov)

Recent multicenter randomized trial of sirolimus vs sirolimus and steroids (*Blood 139 (11) 2022)*

- Lymphatic Anomalies
- KHE/TA
- KLA
- CLVA/KT
- PTEN
- Venous Malformations
- BRBNS
- Not for: AVM, CCLA

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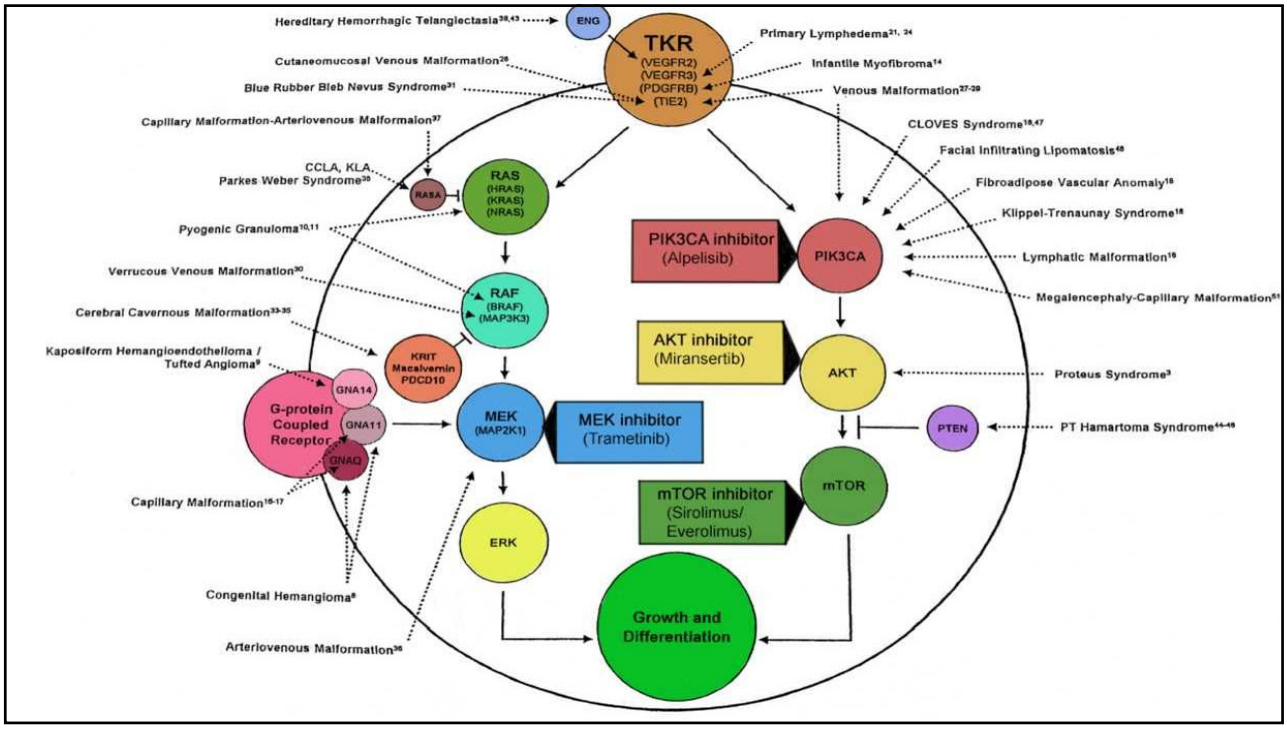

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PHENOTYPE/GENOTYPE CORRELATION

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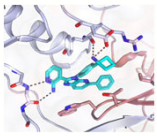

AKT INHIBITORS

- Miransertib
- Mechanism:
  - Binds and inhibits the activity of Akt
  - Inhibition of the PIK3/Akt signaling pathway
- Indications:
  - Breast Cancer
  - Proteus syndrome
  - PROS
- Oral once a day dosing
- PK dosing
- 1/6 dose used in Cancer
- Side Effects: well-tolerated
  - Mouth Sores
  - Headaches
  - GI complaints
  - Metabolic issues
  - Anemia
  - Hyperlipidemia
  - Pneumonitis
- MOSAIC Study (Proteus and PROS) is active but not recruiting
- Study of Safety and Tolerability in Patients with PROS and Proteus Treated with Miransertib (MK-7075) (MK-7075-006)
- Other AKT inhibitors are in investigation

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ALPELISIB

- Oral PIK3CA inhibitor for PROS
  - Selectively inhibits Class I PI3K p110α (catalytic subunit)
  - Lipid kinase that plays a role in biological processes, proliferation, survival , differentiation and metabolism
  - FDA approved for metastatic and recurrent Breast Cancer in combination with other therapy
  - **Recent FDA approval for PROS (contingent on EPIKP2)**
  - **Recent reports of efficacy in Venous Malformations at ISSVA 2022**
- Side Effects: Hyperglycemia, Diarrhea, Skin, Mouth sores, Alopecia
- Studies Available
  - MAP Alpelisib for PROS
  - Retrospective Chart review (completed) – EPIK-P1
  - Prospective, Double Blind upfront 16 week placebo controlled trial to assess efficacy and safety of Alpelisib in Pediatric and Adult patients – EPIK-P2
    - Group I 18 years and older
    - Group II 6-17 years
    - Group III 2-5 years
    - Starting dose for Group I 125 mg a day
    - Starting dose for Group II 50 mg a day

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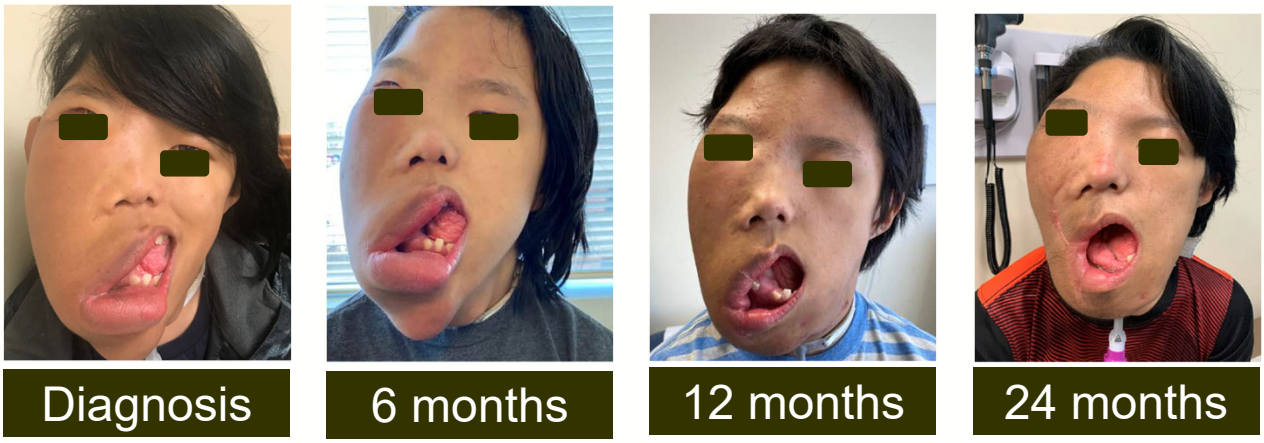

TREATMENT WITH ALPELISIB

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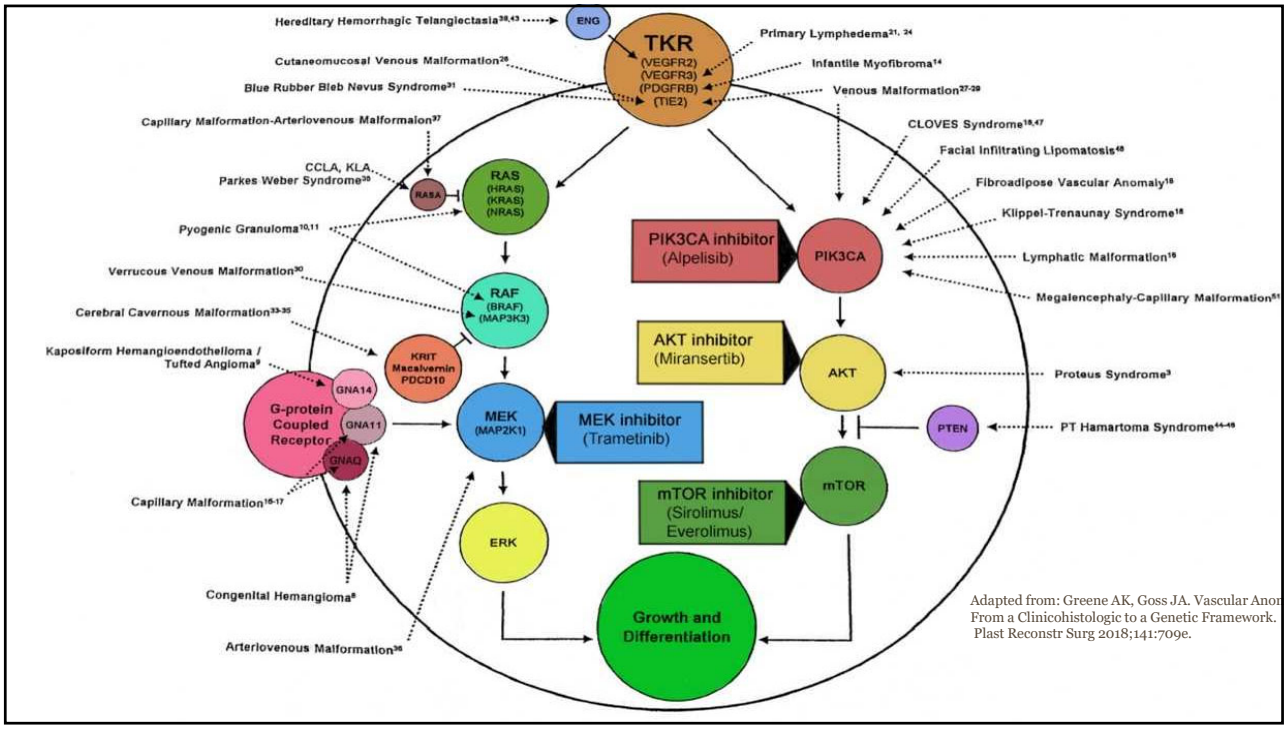

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MEK INHIBITORS

- Trametinib
  - Reversible MEK1/2 inhibitor
  - Approved for BRAF mutated melanoma, non-small cell lung cancer, anaplastic thyroid Cancer
  - Being studied in Pediatric brain tumors, LCH, Juvenile Myelomonocytic Leukemia, infantile cardiomyopathy associated with RAS-pathway mutations
  - Side Effects: Skin, GI, Cardiac, ophthalmologic
  - Reported cases at ISSVA with good results. Most adults with skin toxicity and only can tolerated 1mg – 1.5 mg a day. Liquid dosing available for children but need IND
- Cobimetinib In Extracranial Arteriovenous Malformations (COBI-AVM Study, Arkansas)
- Selumetinib Approved in NF patients
- Trametinib in Extracranial Arteriovenous Malformations (Stanford, UCSF)
- CaNVAS Genotype Phenotype study with Trametinib

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RASOPATHIES

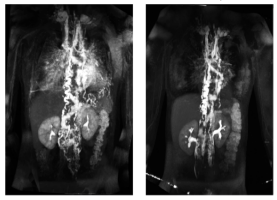
Patient 3: 18 yo with KLA and CBL Mutation

Outcome:

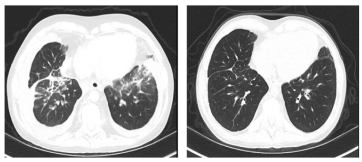
- Normalization of respiratory and clotting parameters
- Complete remodeling of central lymphatic system
- Normalization of chest CT and resolution of effusion

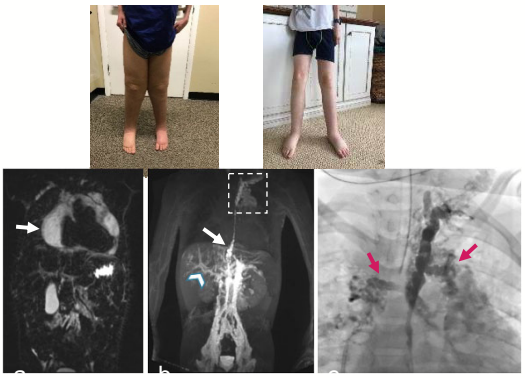
Parameter	Baseline	Post Treatment
FEV1 (% predicted)	53	89
FVC (% predicted)	56	81
TLC (% predicted)	67	87
Platelets (K/μL)	568	231
D-dimer (μg/mLFEU)	9.17	<0.27

DCMRL pre DCMRL post



DCMRL pre DCMRL post





Noonan Syndrome
KLA
AVM
CCLA
Rasa-1

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OTHER THERAPIES

- Topical VT30 (PIK3CA inhibitor)
  - Venous/Lymphatic malformations with PIK3CA or TEK mutations
  - Age 18-60
  - Multiple biopsies
  - Phase I
  - Phase II
- PALV-06 Topical Sirolimus 3.9% gel (PTX-022)
  - Phase II
  - Treatment of microcystic lymphatic malformations
  - 13 and older

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Vascular Anomaly	Gene	Treatment
Venous Malformation	TEK PIK3CA	TIE-2 Inhibitors Alpelisib
PROS	**PIK3CA**	**Alpelisib, mTOR inhibitors**
PHTS	PTEN	mTOR inhibitors
HHT	ENG, ALK1 HHT3, HHT4 GDF2or BMP9	Bevacizamab Thalidomide/derivatives Pazopanib
GSD	**KRAS**	**MEK Inhibitors, mTOR inhibitors with bisphosphonates**
KLA	**NRAS** **CBL**	**MEK Inhibitors, mTOR inhibitors**
CM-AVM1 CV-AVM2	RASA1 EPHB4	?MEK Inhibitors
AVM	MAP2K1 KRAS BRAF	MEK inhibitors Thalidomide
Congenital Hemangiomas	GNAQ GNA11	GNAQ inhibitors
Pyogenic Granulomas	GNAQ,KRAS,HRAS, BRAF, GNA14	?BRAF inhibitors, MEK inhibitors

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NEW THERAPEUTICS

- Goal is to reduce not eliminate: we need to support normal growth
- We do not need the MTD
- Use of medication will be chronic thus the toxicity profile of a drug is important (short and long term)
- We will be treating Children and Adults
- Cancer Diagnoses may learn from VA

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THOUGHTS FOR THE FUTURE

Need for more Natural History Data	Improved Outcome Measures for Clinical Trial	Adaptive Study Design	Preclinical Testing
Animal models	Availability of genomic testing For all	Circulating free DNA	Improvement of NIH Funding
Awareness	Collaboration Nationally and Internationally	Industry support	Drug Delivery

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Anticoagulation QOL

PedsQL™

Laboratory and QOL monitoring in Slow Flow Vascular Anomalies

CANVAS

Team LULABI


Prospective Cohort Study in Complex Lymphatic Anomalies

NKKDRV Vwxg|

Kaposiform Hemangioendothelioma: Hematology and Oncology Survey Study

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SECURE-VA REGISTRY

Surveillance Epidemiology of Coronavirus (COVID-19) Under Research Exclusion

VATCH

Genotype/Phenotype Matching for Vascular Anomalies

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THE POWER OF THE PATIENT'S VOICE

- An individual patient can catalyze important clinical & scientific collaboration "The Power of One"
- We the community can and should contribute to patient care and research
- Each of us can support our rare disease cause using whatever skills and background experience that we have

IP DJIQH# KDW# L# DQ# DFFRP SOLVK# WRJHWKHU

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WHEN YOU HEAR HOOF BEATS FIRST THINK HORSES BUT DON'T FORGET THE ZEBRAS

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THANK YOU

- Patients and Families
- Patient and Family Support Groups: LMI, LGDA, KT support Group, Cloves Syndrome Community, NOVA, HHT support Group
- Funding Sources: FDA, NIH, LMI
- Institutional Support: Frontier Program, Hospital and Divisions

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