Overview of Rare Bone Diseases

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Past Chair
Rare Bone Disease Alliance Steering Committee
Disclosures:

Leadership:
US Bone & Joint Initiative – BOD
American Bone Health – Scientific Advisory Board
American Orthopaedic Association – “Own the Bone” Steering Committee
Patient Centered Outcomes Research Institute (PCORI) – Rare Disease Advisory Council
FDA Science Board

Research:
Grant funding from NIH, PCORI, Ultragenyx
Overview

• Organizing one’s thinking about rare bone diseases
• Personal Game Changers
• Rare Bone Disease Alliance
• RBDA TeleECHO
• Things I am excited about
RARE DISEASES: An Overview

• Rare Diseases:
  • affecting fewer than 200,000 US residents, or
  • those without reasonable expectation that drug development costs will be recoverable by US sales.

• >6400 rare diseases estimated to affect 18-30 million US residents
Nosology and classification of genetic skeletal disorders: 2019 revision

Geert R. Mortier | Daniel H. Cohn | Valerie Cormier-Daire | Christine Hall
Deborah Krakow | Stefan Mundlos | Gen Nishimura | Stephen Robertson
Luca Sangiorgi | Ravi Savarirayan | David Sillence | Andrea Superti-Furga
Sheila Unger | Matthew L. Warman
Genetic skeletal disorders

- Dysplasias
- Metabolic
- Dysostoses
  Reduction defects

- First nosologies were in 1969, 1970, 1971
  - Not all with short limbs had achondroplasia or short trunk had Morquio
  - Victor McKusick, Charles Scott, Dave Rimoin et al
- 10th version in 2019
- 461 genetic skeletal disorders
  - 42 groups: molecular, biochemical, radiography
  - 437 genes associated with 425 of these disorders (92%)
What does the Nosology do?

Helps me organize my thoughts

• common underlying gene or pathway

• the localization of radiographic abnormality, e.g. (vertebrae, epiphyses, metaphyses, diaphysis, or combination)

• combination with clinical and radiographic findings (bent bones, slender bones, presence of multiple dislocations)

• features of mineralization (increased or reduced bone density, impaired mineralization, stippling, osteolysis)
How many people are we really talking about?

- ~5% of rare disorders
- <5 per 10,000 individuals
- All told, likely less than 200,000 individuals in the US
  - OI 25-50,000
  - Achondroplasia ~15,000
  - XLH 10-15,000
  - FOP <1,000 worldwide
  - Jansen’s perhaps 30 cases identified
Rare Bone Disease
Personal Game Changers:
Adults with childhood onset disorders population exploding
LIVE TO 100 and love every minute
Our long-life experts tell you how
LONGLVITY QUIZ P. 33

Sophia's AGE-DEFYING SECRETS
Almost no centers prepared to provide adult care
More patients are being identified

Improving the “Diagnostic Odessey”
Registries

Natural History Studies
Leveraging virtual communication to advance PCOR adoption by the rare bone disease community

Goal: strengthen the working relationships among members of the Rare Bone Disease Alliance (RBDA).

- Many rare bone diseases have similarities
  - Significant “shared knowledge”
  - Shared experts
  - Shared experiences
Bone is rarely the only issue
History:

Rare Bone Disease Patient Network founded in 2006

Morphed: Rare Bone Disease Alliance 2017

Currently: 15 rare bone disease member organizations

26 scientists RBDA’s scientific panel.
The **mission** of the RBDA is to educate professionals, expand research, and assist patients and communities affected by rare bone diseases.

Collaboration ... sharing

Grass roots .... Supported and led by leaders of advocacy groups and academics from across a wide spectrum of universities

Reduce the length of the “diagnostic odyssey”
Inspiration

OIF CEO Tracy Hart
Launched August 2019

Project ECHO®

Rare Bone Disease

Expanding capacity for health outcomes
ECHO is not Telemedicine
<table>
<thead>
<tr>
<th>Date</th>
<th>Speaker Name</th>
<th>Main Presentation Title</th>
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<tbody>
<tr>
<td>August 5, 2021</td>
<td>Matthew Warman, MD</td>
<td>Differential Diagnosis of Overgrowth conditions</td>
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<tr>
<td>September 2, 2021</td>
<td>Patty Dickson, MD</td>
<td>Skeletal Presentations of Lyosomal Storage Diseases</td>
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<tr>
<td>October 7, 2021</td>
<td>Fred Singer, MD</td>
<td>Paget’s disease of bone</td>
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<td>November 4, 2021</td>
<td>Danita Velasco, MD</td>
<td>The Dysmorphology Exam for Skeletal Dysplasias</td>
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<tr>
<td>December 2, 2021</td>
<td>Cathleen Raggio, MD</td>
<td>Pulmonary Challenges in OI</td>
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<tr>
<td>January 6, 2022</td>
<td>Emily Farrow, PhD, CGC</td>
<td>Genetic Testing – Emerging Diagnostic Technologies</td>
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<tr>
<td>February 3, 2022</td>
<td>Rachel Gafni, MD</td>
<td>Hypoparathyroidism</td>
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<tr>
<td>March 3, 2022</td>
<td>Michael Whyte, MD</td>
<td>Dense Bone Diseases: Too Much Of A Bad Or Good Thing</td>
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<tr>
<td>April 7, 2022</td>
<td>Zvi Grunwald, MD</td>
<td>FOP and anesthesia</td>
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<tr>
<td>May 5, 2022</td>
<td>Sherri-Ann Burnett-Bowie, MD, MPH</td>
<td>Differential Diagnosis of Non-XLH FGF 23 Disorders</td>
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<tr>
<td>June 2, 2022</td>
<td>Michael Bober, MD, PhD</td>
<td>Achondroplasia</td>
</tr>
<tr>
<td>July 7, 2022</td>
<td>Nina Ma, MD</td>
<td>MCTO</td>
</tr>
</tbody>
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~ half disease specific
~ half differential diagnosis
International Registrations

- United States: 807, 69%
- International: 359, 31%
• Meet monthly, first Thursday of the month, 3pm - 4:30
• Zoom technology
• Need to pre-register
• Free event, free CME
• Open to all clinicians, not aimed at patients
• Didactic portion ONLY of programs recorded and available on YouTube

• >20,000 downloads to date

• In addition: OI and SoftBones launched their own TeleECHOs; programs available through their websites
So, what am I excited about?
Group 1: Fibroblast growth factor receptor type 3 (FGFR3)  
Chondrodysplasia Group

- about 1 in every 25,000–30,000 individuals
  - translates into around 250,000 affected persons worldwide
- autosomal dominant
  - mutations are fully penetrant and show only modest variability of expression.
- most instances of achondroplasia – perhaps 80% – arise from new, spontaneous mutations

Pauli RM.  
Achondroplasia: a comprehensive clinical review. Orphanet J Rare Dis. 2019
Achondroplasia Natural History Study (CLARITY): a multicenter retrospective cohort study of achondroplasia in the United States
Novel therapeutic approaches for Rx Achondroplasia

- There are 4 Investigation Products being trialed in children with ACH
  - CNP agonist – short acting
  - CNP agonist – long acting
  - Soluble FGF3 decoy
  - Tyrosine Kinase inhibitor
Focus NOT Height
foramen magnum
cervical and lumbar stenosis
• **Cortical and Trabecular Bone (Both)**
  Carbonic anhydrase II deficiency
  Dysosteosclerosis
  Lenz-Majewski syndrome
  Hepatitis C-associated osteosclerosis
  Osteopetrosis
  Pycnodysostosis

• **Cortical Bone (Predominantly)**
  Autosomal dominant osteosclerosis
  Diffuse idiopathic skeletal hyperostosis
  Endosteal hyperostosis
  van Buchem disease
  sclerosteosis
  Hypertrophic osteoarthropathy
  Pachydermoperiostosis
  Progressive diaphyseal dysplasia
  (Engelmann disease)

• **Trabecular Bone (Predominantly)**
  Dysplastic
  Central osteosclerosis with ectodermal dysplasia
  Osteomesopyknosis

**Hematological**
  Mastocytosis
  Myelofibrosis
  Polycythemia vera
  Sickle cell disease

**Metabolic**
  Fluorosis,
  Hyperparathyroidism,
  Renal osteodystrophy,
  X-linked hypophosphatemia
  Vitamin D toxicity

**Neoplastic Disorders**
  Metastatic disease
  Myeloma, lymphoma, leukemia

Group 23
Increased bone density
Osteopetrosis – decreased bone resorption

- Osteopetrosis = stone-like bone
- Two types
  - Osteoclast-rich = functional defect in cells
  - Osteoclast poor – reduced number
- Genetic types multiple includes RANKL, LRP5
  - Autosomal dominant 1:100,000 “benign”
  - Recessive/malignant 1:500,000
- Clinically
  - Increased bone density
  - Frequent fractures
Toulouse Lautrec
Pycnodysostosis
An osteoclast-rich osteopetrosis
<table>
<thead>
<tr>
<th>Subspeciality</th>
<th>Complication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Endocrinology</td>
<td>Osteopetrosis&lt;br&gt;Hypocalcemia</td>
</tr>
<tr>
<td>Ophthalmology</td>
<td>Papilledema&lt;br&gt;Ptosis&lt;br&gt;Strabismus&lt;br&gt;Paralysis of extraocular muscles&lt;br&gt;Optic nerve atrophy&lt;br&gt;Exophthalmos&lt;br&gt;Nystagmus&lt;br&gt;Retinal degeneration&lt;br&gt;Tearing (from nasolacrimal duct obstruction)</td>
</tr>
<tr>
<td>Dentistry</td>
<td>Delay/failure of tooth eruption&lt;br&gt;Malformed crowns/roots&lt;br&gt;Periodontal ligament defects&lt;br&gt;Odontoma&lt;br&gt;Tooth agenesis&lt;br&gt;Enamel hypoplasia&lt;br&gt;Tooth decay/caries&lt;br&gt;Thickened lamina dura&lt;br&gt;Osteomyelitis (most frequently of the mandible)</td>
</tr>
<tr>
<td>Orthopedics</td>
<td>Skeletal deformities&lt;br&gt;Scoliosis&lt;br&gt;Spondylolisthesis&lt;br&gt;Fractures (particularly of the long bones)&lt;br&gt;Delayed union/nonunion&lt;br&gt;Degenerative arthritis&lt;br&gt;Spondyloysis</td>
</tr>
<tr>
<td>Neurology/neurosurgery</td>
<td>Compressive cranial neuropathies (often optic and facial nerves, but can involve any of cranial nerves I–VIII)&lt;br&gt;Increased intracranial pressure&lt;br&gt;Craniosynostosis&lt;br&gt;Ardor–Chiari I malformation&lt;br&gt;Neuromuscular scoliosis&lt;br&gt;Developmental delay/regression, seizures (OSTM1 mutation)&lt;br&gt;Calcifications of the basal ganglia, thalami (CALI deficiency)&lt;br&gt;Hydrocephalus&lt;br&gt;Cerebrovascular stenosis/occlusion&lt;br&gt;Acquired encephalocele</td>
</tr>
<tr>
<td>Otolaryngology</td>
<td>Conductive hearing loss&lt;br&gt;Recurrent otitis media&lt;br&gt;Chronic congestion (poorly pneumatized sinuses)&lt;br&gt;Rhinorrhea&lt;br&gt;Choanal atresia&lt;br&gt;Rhinosinusitis&lt;br&gt;Obstructive sleep apnea</td>
</tr>
<tr>
<td>Hematology</td>
<td>Thrombocytopenia with bleeding&lt;br&gt;Anemia&lt;br&gt;Leukopenia with frequent infections&lt;br&gt;Hepatosplenomegaly&lt;br&gt;Transfusion dependence</td>
</tr>
<tr>
<td>Nephrology</td>
<td>Renal tubular acidosis, nephrocalcinosis, and nephrolithiasis (CALI deficiency)</td>
</tr>
</tbody>
</table>
Diagnosis and Management of Osteopetrosis: Consensus Guidelines From the Osteopetrosis Working Group

Group 25 Osteogenesis Imperfecta and decreased bone density

Osteogenesis Imperfecta (OI)

- “brittle bone disease”
- Low bone mass, increased bone fragility, bone deformity, growth deficiency, joint hypermobility
- 1: 15-20,000 births
Osteogenesis imperfecta (OI)

Estimated prevalence ~1 in 15,000

Skeletal features:
• Low bone mineral density
• Recurrent fractures
• Skeletal deformities
• Dentinogenesis imperfecta

Extraskeletal features:
• Hearing loss
• Pulmonary abnormalities
• Muscle weakness

Cheung et al., Rev Endocr Metab Disord 2008
Original 1979 Sillence classification: 4 OI types

Dominant forms
~ 90% cases

COL1A1
COL1A2

Recessive Forms
~10% cases

CRTAP
LEPRE1
PPIB
SERPINH1
FKBP10
SERPINH2
SERPINF1
SP7
BMP1
WNT1
## TYPING OF OSTEOGENESIS IMPERFECTA - CURRENT

### Table: Nosology of Osteogenesis imperfecta

<table>
<thead>
<tr>
<th>Osteogenesis imperfecta type</th>
<th>Inheritance</th>
<th>Phenotype</th>
<th>Gene Defect</th>
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</thead>
<tbody>
<tr>
<td><strong>Defects in collagen synthesis, structure or processing</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>AD</td>
<td>Mild</td>
<td>Null COL1A1 allele</td>
</tr>
<tr>
<td>II</td>
<td>AD</td>
<td>Lethal</td>
<td>COL1A1 or COL1A2</td>
</tr>
<tr>
<td>III</td>
<td>AD</td>
<td>Progressive deforming</td>
<td>COL1A1 or COL1A2</td>
</tr>
<tr>
<td>IV</td>
<td>AD</td>
<td>Moderate</td>
<td>COL1A1 or COL1A2</td>
</tr>
<tr>
<td>XIII</td>
<td>AR</td>
<td>Mild to severe</td>
<td>BMP1</td>
</tr>
<tr>
<td><strong>Defects in bone mineralization</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>V</td>
<td>AR</td>
<td>Variable, distinctive histology</td>
<td>IFITM5</td>
</tr>
<tr>
<td>VI</td>
<td>AR</td>
<td>Moderate to severe</td>
<td>SERPINF1</td>
</tr>
<tr>
<td><strong>Defects in collagen modification</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VII</td>
<td>AR</td>
<td>Severe (hypomorph)</td>
<td>CRTAP</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Severe to lethal (null)</td>
<td></td>
</tr>
<tr>
<td>VIII</td>
<td>AR</td>
<td>Severe to lethal</td>
<td>LEPRE1</td>
</tr>
<tr>
<td>IX</td>
<td>AR</td>
<td>Moderate to lethal</td>
<td>PPIB</td>
</tr>
<tr>
<td>XIV</td>
<td>AR</td>
<td>Severe</td>
<td>TMEM38B</td>
</tr>
<tr>
<td><strong>Defects in collagen folding and cross-linking</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>X</td>
<td>AR</td>
<td>Severe to lethal</td>
<td>SERPINH1</td>
</tr>
<tr>
<td>XI/BRKS1</td>
<td>AR</td>
<td>Mild to severe</td>
<td>FKBP10</td>
</tr>
<tr>
<td>BRKS2</td>
<td>AR</td>
<td>Moderate to severe</td>
<td>PLOD2</td>
</tr>
<tr>
<td><strong>Defects in osteoblast development with collagen insufficiency</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>XII</td>
<td>AR</td>
<td>Severe</td>
<td>SP7</td>
</tr>
<tr>
<td>XV</td>
<td>AR</td>
<td>Severe</td>
<td>WNT1</td>
</tr>
<tr>
<td>XVI</td>
<td>AR</td>
<td>Severe</td>
<td>CREB3L1</td>
</tr>
</tbody>
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Published on OIF website
Natural History Studies and Clinical Trial Readiness: Brittle Bone Disorders Consortium (BBDC)

• Brendan Lee, MD, PhD (on behalf of BBDC Investigators)
• Baylor College of Medicine
The National Institutes of Health (NIH) Rare Diseases Clinical Research Network (RDCRN).

- (1) collaborative clinical research in rare diseases, including longitudinal studies, clinical studies, and clinical trials;
- (2) training of clinical investigators in rare diseases research;
- (3) proof-of-concept clinical research projects; and
- (4) access to information related to rare diseases for researchers, physicians, health care professionals, patients, and the general public.
Take home lessons

• Largest sample sizes to date to inform clinical endpoints relevant to clinical trial readiness

• Discover clinical signals not previously appreciated or studied
  • Postpartum hemorrhage
  • Pain and anxiety

• Effect sizes for different subtypes of OI (addresses variable expressivity that confounds sample size) – Growth, PFTs, Mobility, Hearing Loss, QOL, etc.

• Broad connective tissue targets beyond bone

• Basis for both academic and industry partners in clinical trial design and feasibility
  • BBDC Fresolimumab – Sanofi/Genzyme
  • Industry sponsored - Mereo/Ultragenix and Amgen
Hypophosphatasia

• Inborn error of metabolism
  • Loss of function mutation in the ALPL gene which encodes tissue nonspecific alkaline phosphatase
  • Defective mineralization
• Extremely variable
  • Perinatal lethal to dental manifestations only
• Clinically
  • Decreased alk phos activity with elevation vitamin B6 and phosphoethanolamine
<table>
<thead>
<tr>
<th>Clinical Types of Hypophosphatasia</th>
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<tbody>
<tr>
<td>Perinatal</td>
<td>In utero and at birth</td>
</tr>
<tr>
<td>Infantile</td>
<td>&lt;6 months</td>
</tr>
<tr>
<td>Childhood/juvenile</td>
<td>&gt;6 months to &gt;18 years</td>
</tr>
<tr>
<td>Adult</td>
<td>&gt;18 years</td>
</tr>
<tr>
<td>Odontohypophosphatasia (dental only)</td>
<td>Any age</td>
</tr>
</tbody>
</table>
Prevalence of HPP: AR and also Milder Forms

Canada (Toronto): incidence 1:100,000 live births (local data extrapolated)

France: prevalence 1:300,000 (molecular testing)

Japan: prevalence of a founder mutation (c.1503G>A)
1:900,000 (genetic analysis)

Canada (Winnipeg, Mennonite population): incidence of homozygous founder missense mutation (1:25) resulting in 1:2,500 live births

Germany: incidence 1:4:500,000 (ESPED survey; 2003 population)

Europe: prevalence 1:538,000 (molecular testing; 20 countries included)
Prevalence of Rare Bone Dysplasias

XLH has an estimated prevalence of 1:20,000 to 1:25,000.

There are 12,000 to 16,000 XLH patients in the US.

The prevalence per 100,000 people is as follows:
- OI: 7.75
- XLH: 5.0
- HPP: 0.33

Prevalence data for OI and XLH were global, while prevalence data for HPP were specific for severe forms of the disease within the EU. XLH = X-linked hypophosphatemia; OI = osteogenesis imperfecta; HPP = hypophosphatasia; US = United States; EU = European Union.

Skeletal survey
Age 1 day

12 months
Potential Systemic Manifestations of HPP in Adults:

Skeletal
- Chronic bone inflammation
- Recurrent, nontraumatic, nonhealing, or low-trauma fractures
- Subtrochanteric or metatarsal fractures
- Pseudofractures
- Osteomalacia
- Osteopenia
- Short stature
- Bowed legs
- Bone pain

Physical Function
- Loss of physical function impacting activities of daily living
- Unusual gait
- Impaired mobility (including need for assistive devices such as wheelchair, walker, crutches, or cane)

Dental
- Adult tooth loss
- Abnormal dentition
- Periodontal disease
- History of premature tooth loss

Muscular/Rheumatologic
- Muscle and joint pain
- Muscle weakness
- CPPD disease/pseudogout/chondrocalcinosis
- Calcific periarthritis

Renal
- Renal failure
- Kidney stones
- Nephrocalcinosis

Clinical presentation in Adult: HPP is heterogeneous

XLH Hypophosphatemic Rickets

• Originally described as “vitamin D-resistant rickets”
• Genetic form of rickets
• Loss of function pathogenetic variants in the PHEX gene
  • Over expression phosphaturic protein fibroblast growth (FGF23)
• Hyperphosphaturia (impaired renal tubular phosphate reabsorption) leads to hypophosphatemia and rickets
  • Also dental abscesses, craniosynostosis, motor delay
• Traditionally treat with phosphate salts and calcitriol = POOR COMPLIANCE
• Now anti-FGF23 monoclonal antibody
But straight bones are not enough

Challenges in adulthood include:

- Arthritis
- Hyperparathyroidism
- Osteophytes
- Calcified entheses
- Spinal stenosis
- Hearing loss
- Myopathy
- Dental abscesses
Historically stopped treatment in adulthood due to the complications of long term traditional therapy

But histomorphology demonstrates that the osteomalacia will persist

Treatment throughout the lifespan be should be considered

But, likely will not improve all aspects
An Evidence-based Physical Therapy Prescription for Adults With X-linked Hypophosphatemia
Karthik Kanamalla,¹ Rebekah Fuchs,² Casey Herzog,² Keith D. Steigbigel,¹ and Carolyn M. Macica¹,⊥

Link to specific exercises  reference #18
Group 27 Disorganized development of skeletal components

Fibrous Dysplasia/McCune-Albright syndrome:
A complex, mosaic disorder of $G_\alpha_s$ activation

Bone, endocrine, skin & other
Clinical Pearls

FD lesions are established in a predictable, age-related pattern

• Staging evaluation at age 5 will identify all areas of clinically significant FD

FD lesions are highly sensitive to effects of endocrinopathies

• Early diagnosis & aggressive management of even mild endocrine disease can improve skeletal outcomes
Endocrinopathies Increase Skeletal Morbidity in Fibrous Dysplasia

Hypophosphatemia: Fractures

- low %TRP
- normal %TRP

Fracture rate (mean vs. age in years)

Pan, JBMR 2018
N=158

Normal skull base
FD: Displaced cervical vertebrae

Hyperthyroidism, Hypophosphatemia: Basilar Invagination

Leet, JBMR 2004
N=35

Hyperthyroidism, Hypophosphatemia: Scoliosis

Berglund, JBMR 2018
N=138

GH Excess: Vision loss, Hearing loss

Amit, PLOS One 2011
N=122

Boyce, JAMA-Oto 2017
N=130
Best practice management guidelines for fibrous dysplasia/McCune-Albright syndrome: a consensus statement from the FD/MAS international consortium
Fibrous Dysplasia Ossificans Progressiva

- ~1000 individuals worldwide or 0.5/million
- Mutation in the gene ACVR1 (also known as activin-like kinase 2 (ALK2))
- Abnormal activation of ACVR1 leads to transformation of connective tissue and muscle tissue into a secondary skeleton.
Key Clinical Recommendations

- Great toe malformations + migratory swellings should raise possibility of FOP
- If FOP is suspected, avoid trauma and biopsies until diagnosis of FOP is ruled out
  - NO BIOPSIES!!
  - Routine medical care with peripheral IVs is OK
- Contact a major FOP clinical center for guidance – Especially if intubation is needed
  - See IFOPA or the FOP ICC for listing of sites
Identifying and engaging companies
Patient Engagement
Financial Contributions
Clinical Trial Communication
Patient Privacy
Key resources:

• The FOP Treatment Guidelines:  

• The International FOP Association – www.ifopa.org

• The International Clinical Consortium on FOP – www.iccfoporg

• Clinical trial recommendations for FOP  
Gorham Stout
aka Disappearing or Vanishing Bone Disease

• Can appear at any age
• Typically affects jaw, clavicle, ribs, pelvis. Femur and neck vertebrae
• Progressive osteolysis and replacement with fibrous tissue
• Intense pain and disability
• Not clear that this is an osteoclast disorder but osteoblasts do not help out
• Sirolimus (immunosuppressent) Rx plus bisphosphonate

August 31, 2022
Group 30 Overgrowth Syndromes with Skeletal Involvement

Proteus Syndrome
PIK3CA Mutations: CLOVE syndrome

congenital
lipomatous
overgrowth
vascular malformations
epidermal nevi
Tumor Induced Osteomalacia - TIO

Upregulation of FGF23 →
chronic hypophosphatemia →
increased renal phosphate excretion →
dysregulated vitamin D metabolism →
widespread osteomalacia and fractures
Surgery cures but sometimes the tumor can’t be found
Conventional treatment of TIO with phosphate + active vitamin D

- Does not address underlying cause of hypophosphatemia
- Requires frequent monitoring due to risk of nephrocalcinosis, hypercalciuria, hyperparathyroidism

Burosumab anti-FGF23 treatment

- Improves hypophosphatemia, bone health, pain, physical functioning

WE WANT YOU!
Thank You