Understanding Disease Background and Hallmark Symptoms of Fibrodysplasia Ossificans Progressiva (FOP)

Clinical Pearls: Hallmark FOP Symptoms

Check the toes

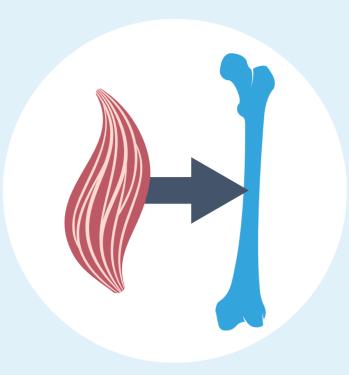
Use caution with invasive procedures

Great toe malformations are always seen at birth in classic FOP (eg, hallux valgus), even if a newborn otherwise appears normal. Some diagnostic procedures (eg, biopsy) can cause explosive heterotopic ossification (HO) formation in patients with FOP.

Note unusual neck stiffness

Patients with FOP often develop neck stiffness in early childhood, which can make crawling difficult for them.

FOP Is an Ultra-Rare Genetic Condition



FOP causes progressive, disabling conversion of connective tissue and muscle to bone.



Worldwide prevalence is estimated to be between 0.5 and 1.4 per million with **no ethnic, racial, gender, or geographic predilection.**



FOP is a debilitating disease with distinct clinical characteristics, yet is difficult to diagnose. **Diagnostic delay and erroneous diagnosis are common.**

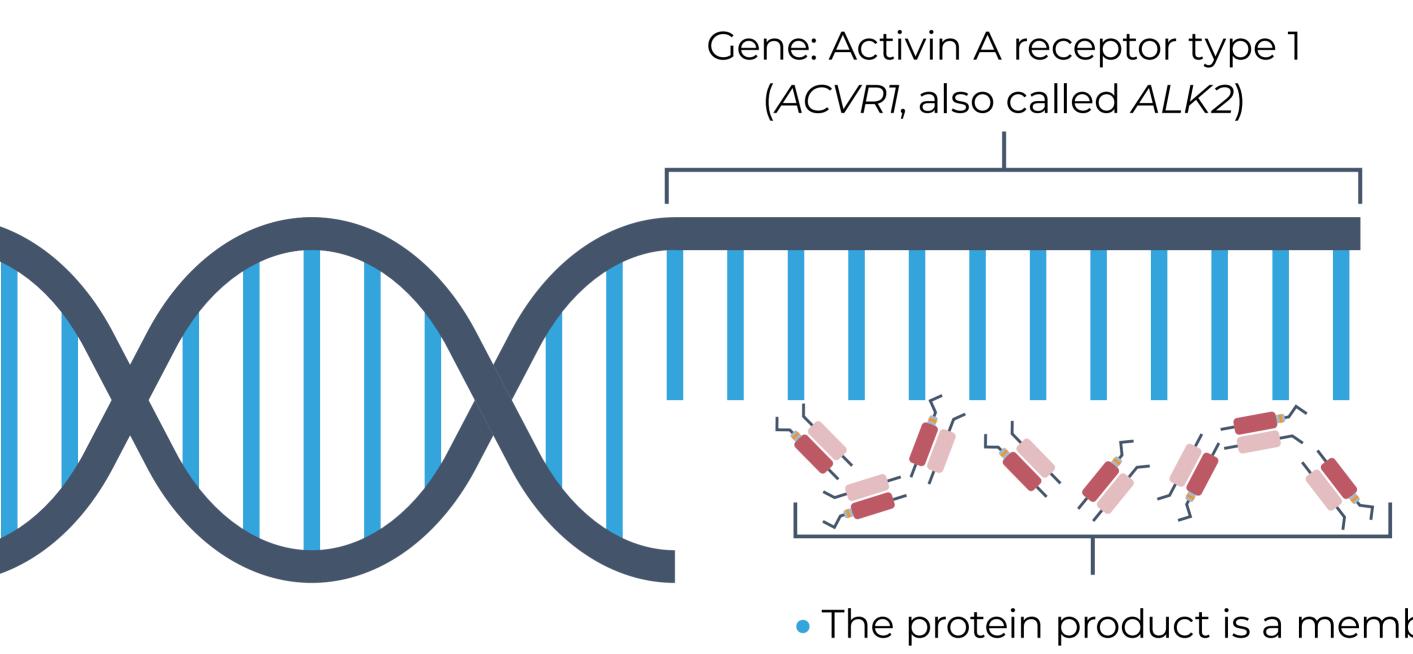


During the diagnostic journey, patients with FOP often have dangerous and unnecessary diagnostic procedures that lead to permanent harm and lifelong disability.



Heightened awareness of FOP and its hallmark symptoms can **hasten an accurate diagnosis** for patients. Heightened awareness of FOP opens the door to expert **resources and treatments needed to provide appropriate and individualized care.**

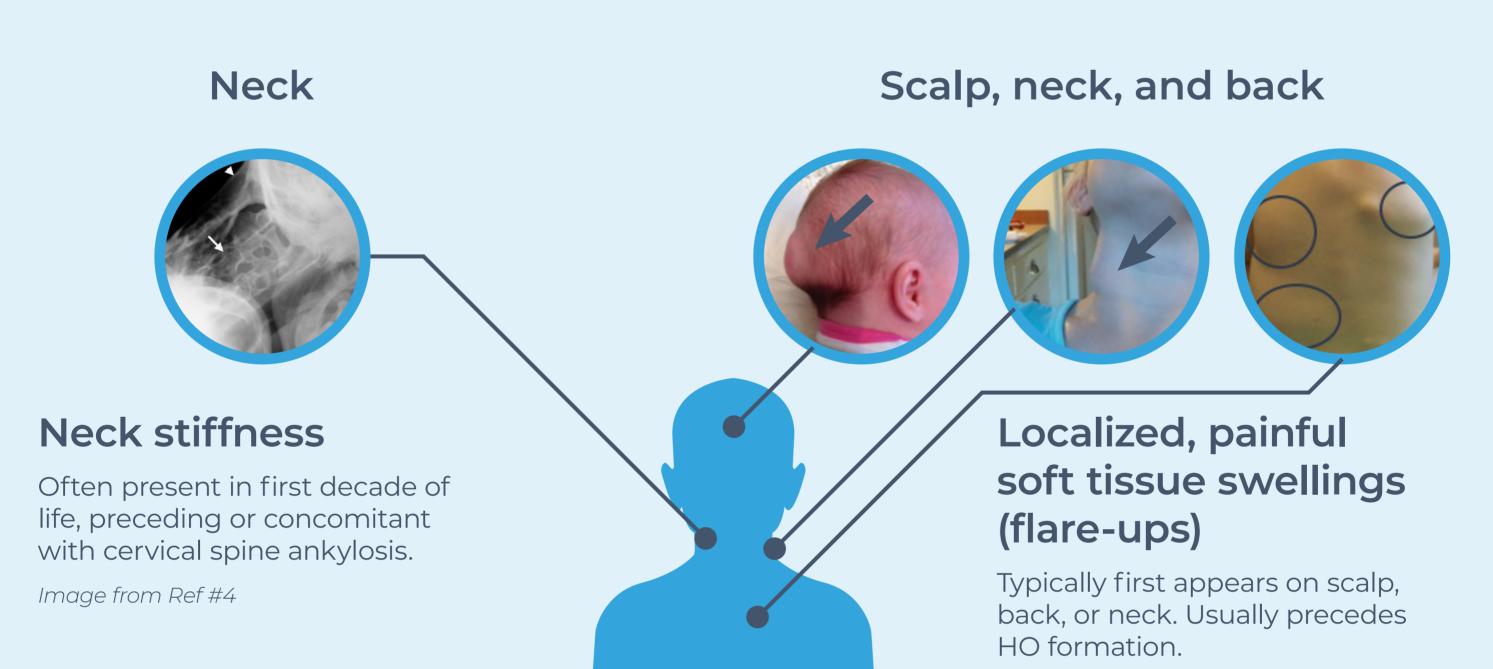
FOP Has a Genetic Cause



- The protein product is a member of the bone morphogenetic protein (BMP)/transforming growth factor beta (TGFβ) receptor family
- Protein has a role in skeletal development, chondrogenesis, and osteogenesis

All ACVR1 pathogenic variants (mutations) that lead to FOP are activating mutations resulting in dysregulated BMP signaling.

There Are Specific Early Signs and Symptoms of FOP



Hands



Hand malformations

May also have short malformed thumbs (left) and clinodactyly (right). Images courtesy of:

Frederick S. Kaplan, MD (left) and Edna E. Mancilla, MD (right) Images courtesy of: Robert J. Pignolo, MD, PhD

Toes



Abnormal-appearing toes at birth

Great toe malformations (hallux valgus) **are always present** in classic form of FOP. *Image from Ref #5*

Possible Additional Clinical Findings

Cervical spine malformations

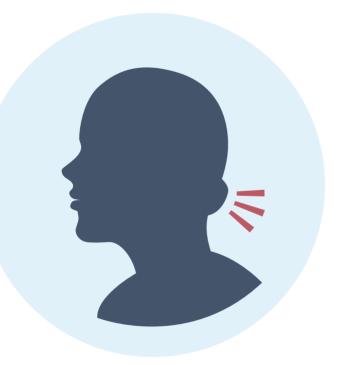
Intra-articular ankylosis of facet joints and early cervical spine degenerative changes

Thumb malformations

Short 1st metacarpal +/- monophalangism

- Short broad femoral necks
- Proximal medial tibial osteochondromas
- Hearing loss

A Timely Diagnosis Prevents or Reduces Harm



Soft tissue swellings can be mistaken for soft tissue sarcoma. Correct diagnosis can reduce need for surgical excision, which can cause explosive HO formation.



Taking fall reduction precautions minimizes trauma that can lead to flare-ups and HO formation.





Implementing prophylactic

measures minimizes respiratory decline (eg, with incentive spirometry). Avoid use of early pharmacologics administered in routes that could cause trauma

(eg, intramuscular injection).



Auditory assessment **identifies any hearing loss to allow for follow-up.**



Regular oral and dental care helps anticipate and manage soft tissue trauma or oral HO formation.

Summary

Understanding the hallmarks of FOP can lead to a timely diagnosis and reduce harm.

Faculty



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Dr. Matthew Drake is an endocrinologist and associate professor of medicine at Mayo Clinic. He has a particular interest in the mechanisms of bone loss and formation in both healthy and disease states.



References

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- 3. Kaplan FS et al. *Hum Mutat.* 2009;30:379-390.
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