Familial Exudative Vitreoretinopathy (FEVR): Blindness, Osteoporosis, and Fractures in Pediatric Populations

2022 Lifespan Research Day Abstract

Research Category: Clinical & Translational

Primary Research Location: Rhode Island Hospital, Department of Orthopedics

Funded By: N/A

Authors(s):

Jake L. Littman, ScM, MPH, Rhode Island Hospital, Brown University. Dept of Orthopedics

Chanika Phornphutkul, MD, Associate Professor, Rhode Island Hospital, Hasbro Children's Hospital, The Miriam Hospital, Brown University. Division of Human Genetics

Celine Saade, MD, Instructor, Rhode Island Hospital, Hasbro Children's Hospital, The Miriam Hospital, Brown University. Dept of Ophthalmology

Elka Arredondo, Doctor of Physical Therapy, DPT, Rhode Island Hospital. Dept of Orthopedics

Marisa Costa, Rhode Island Hospital. Dept of Orthopedics

Roy K. Aaron, MD, Professor, Rhode Island Hospital, The Miriam Hospital, Brown University. Dept of Orthopedics

Abstract

Background & Aim: Familial exudative vitreoretinopathy (FEVR) is a hereditary disorder whose phenotype includes osteoporosis, multiple fractures, and incomplete retinal angiogenesis leading to retinal detachment and blindness. Described herein are the cases of two pediatric siblings who presented to the orthopedic service with multiple fractures and, through multidisciplinary management, were diagnosed and treated appropriately before permanent visual and skeletal impairment. These cases illustrate that genetic diseases should be considered when treating children with multiple fractures, especially when growth disturbances are present.

Methods: One 13−year−old male presented to the orthopedic service for evaluation of a closed distal radius fracture sustained while playing sports. A comprehensive history revealed he had suffered at least four long bone fractures in his lifetime. Physical examination showed height and weight under the 10th percentile and DEXA scan two SD below the mean. Evaluation of his 10−year−old sister revealed a similar history of multiple fractures, with height and weight between 20th and 35th percentiles and DEXA scan two SD below the mean.

Results: Referral to genetic services and whole exome sequencing revealed a variant in both siblings' LRP5 genes. Ophthalmologic examination revealed capillary dropout and a retinal hole in the older sibling's right eye and capillary dropout in the younger sibling's left eye, both consistent with FEVR. The older sibling received laser retinopexy in the right eye as prophylaxis for retinal detachment and retinal tear, and both have since been followed by orthopedic and ophthalmologic services to prevent future sequelae.

Conclusion: LRP5 encodes a transmembrane receptor for Wnt signaling which plays a role in retinal angiogenesis and bone remodeling. Mutations in LRP5 reduce canonical Wnt signaling and lead to osteoporosis and retinal disease characteristic of FEVR. A high index of suspicion by the orthopedic surgeon for genetic diseases is essential when evaluating children with fractures and decreased bone density. Careful analysis of this population can reveal conditions for which interventions and longitudinal management may greatly benefit patients. In these cases, blindness can be avoided and the frequency and consequences of fractures mitigated.

Clinical Implications: (1.) Reduced sequelae in pediatric patients with genetic conditions. (2.) Improved interprofessional expertise.