Fibrodysplasia ossificans progressive (FOP) is a rare genetic disorder characterized by progressive heterotopic ossification of tendons, ligaments and skeletal muscles causing severe deformities and disability. Linear growth and timing of epiphyseal fusion is usually within the normal range. Retinoic acid receptor agonists can have dramatic negative effects on growth and even cause premature growth cessation and epiphyseal fusion (1, 2).

**INTRODUCTION**

**RESULTS**

An 11 5/12-year-old, prepubertal girl with FOP presented in our pediatric skeletal disorders clinic with the concern of early growth cessation. She had participated in a clinical trial of Palovarotene ("MOVE", NCT03312634), a retinoic acid receptor-gamma agonist, since the age of 9 10/12 years. At the visit, she had recently discontinued her participation in the study. During the 18 months on Palovarotene, her height had only increased 1.9 cm to 136.4 cm. A skeletal survey detected fusion of several growth plates that normally remain open until the end of puberty including the growth plates of distal ulna and radius (Fig 2D-E), proximal fibula, distal femur, and proximal humerus (Fig 3). One year after stopping Palovarotene, she was in early puberty and her height had increased another 3.9 cm to 140.3 cm (-2.6 SDS). Measurements of height, sitting height, and arm span (data not shown) confirmed that growth of arms and legs had ceased, whereas growth of the spine continued. Consequently, there was no catch-up growth and instead continuous catch-down growth.

**CONCLUSIONS**

- High-dose retinoic acid receptor agonists can induce premature epiphyseal fusion even before puberty and may therefore cause significant, disproportionate short stature if used in young children.
- The finding that growth of the spine, but not legs and arms, resumed after the treatment was discontinued suggests that long bones are more susceptible than vertebrae to retinoic acid-induced epiphyseal fusion.

**REFERENCES**