Fibrodysplasia Ossificans Progressiva (FOP) is an ultra-rare, disabling genetic disease that causes bone to form in muscle, tendons, ligaments, and other connective tissues. One of the hallmark characteristics of FOP is the malformation of the great toes, which is present in nearly all individuals with FOP. The toe malformation, along with heterotopic ossification, are early signposts for a definitive clinical diagnosis. However, given its rarity, a diagnosis of FOP is often missed at birth and delayed for years. The diagnostic journey has shortened over the last four years, with patients taking on average 1.5 years to receive a correct diagnosis after their first symptom, compared to 2.2 years for participants who were diagnosed prior to 2016. This 33% decrease in age of diagnosis is likely to due to increased overall awareness of FOP due to media coverage, research and drug development activity.

METHOD

The FOP Registry is an international, voluntary, observational study that captures demographic and disease information directly from patients with FOP via a secure web-based tool, and from physicians who are caring for these patients. No experimental intervention is involved. The FOP Registry is a global study available to FOP patients and their physicians worldwide. To encourage global participation, the FOP Registry has been translated into 7 languages: English, French, German, Spanish, Portuguese, Italian and Russian. Before enrolling into the registry, participants must first sign an informed consent and/or assent for minors and confirm their diagnosis of FOP.

Two different data portals have been developed to capture data:

Patient Portal

The Patient Portal allows FOP patients and caregivers to enter information about themselves and their experience living with FOP directly into a web-based tool, and from physicians who are caring for these patients. Two different data portals have been developed to capture data:

Physician Portal

The Physician Portal allows physicians to enter clinical data about patients under their care. Patient data in the Physician Portal may be linked by key identifiers to the corresponding patient data in the Patient Portal.

RESULTS

Data from the FOP Registry shows the mean age of symptom onset to be 6.2 years (range, 0–45), whereas the age at correct diagnosis is 8.3 years (range, 0–48). Diagnosis takes on average longer in those patients who have the variant mutation forms of FOP versus those who have the classic FOP mutation (18.6 vs. 7.0 years).

Prior to receiving a correct diagnosis, patients see on average 3.3 physician specialties (range, 1–10); this average has remained remarkably stable over time. Similar to many rare diseases, misdiagnoses in FOP are common. Slightly over half (52.5%) of FOP Registry participants noted receiving a misdiagnosis. For those who received an incorrect diagnosis, the three most common conditions noted were cancer (20%), juvenile fibromatos (13%) and myositis ossificans (16%). Other erroneous diagnoses include Klippel Feil Syndrome (4%), hallux valgus (3%), and osteochondromas (3%). Orthopedists (25.5%), geneticists (25.1%), and pediatricians (13.7%) are the most common physician specialists providing the definitive diagnosis for FOP. When first symptom onset occurs after the age of 12, rheumatologists (19.0%) play a larger role in providing the correct diagnosis.

Several physician specialties have high rates of misdiagnosis as a ratio of correct diagnoses given. General physicians are 8.9 times more likely to make an incorrect diagnosis for every correct diagnosis given, followed by pediatricians (5.5), orthopedists (2.5), rheumatologists (1.9) and geneticists (0.9). These rates provide a roadmap for further disease awareness education within these medical specialties.

CONCLUSIONS

Patient registries play a prominent role in assisting medical communities to better understand the natural history of rare diseases. Registries can also help these communities better understand the diagnostic journey taken to receive the correct diagnosis, which is critical to ensuring patients receive the proper clinical care and support services. With a misdiagnosis rate over 50%, more disease awareness is essential to increase clinicians’ index of suspicion for FOP.

ACKNOWLEDGEMENTS

We would like to acknowledge and show our sincere gratitude to our registry participants, medical advisory board members, and patient advisory board members for contributing their time and insights to this important research study. The FOP Registry is currently supported by generous funding from our sponsors: Blueprint Medicines, Ipsen, and Regeneron.

CONTACT INFORMATION

To learn more about the FOP Registry, please visit fopregistry.org or fopregistry.org, or email us at help@fopregistry.org.