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EDITORIAL COMMENT

People Have the Power

Fibromuscular Dysplasia Complications*

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"We see this." This is the clinician's mantra to describe a personal experience with an unexplained observation to colleagues, trainees, and patients but which remains uncoded in the taxonomy of medicine. For example, the bifid uvula, which was noted occasionally for decades but was of modest interest until characterized by Loeys et al. (1) and Shprintzen et al. (2) as part of a constellation of signs and symptoms (including widely spaced eyes and aortic aneurysmal disease) resulting from a transforming growth factor-beta receptor (or mothers against decapentaplegic homolog 3 [SMAD3]) mutation. Once findings are grouped into a disease process, the understanding of the disease improves. Increased recognition, aggregation of patients, standardization of descriptions, creation of diagnostic criteria, better estimates of disease incidence and frequency, and systematization of care all flow from identifying a disease that includes the heretofore "we see this" finding.

Fibromuscular dysplasia (FMD) provides a good example of a problem that few clinicians understood or took the time to study. FMD has been recognized as a disorder for 80 years and was known as a secondary cause of hypertension through its effect on the renal arteries (3). It was first described by Leadbetter and Burkland (4) in 1938 in a 5-year-old boy with hypertension resulting from unilateral renal artery involvement. The next great leap in describing FMD came in 1964 when Palubinskas and Ripley (5) registered involvement of arteries other than the renal arteries, identifying involvement of the celiac, superior mesenteric, splenic, and external iliac arteries. In an addendum to the paper, the authors noted the presence of FMD in the internal carotid arteries without renal artery involvement. Then, stagnation. Fifty years later, in a premier textbook on vascular disease, FMD was described as a "generic term for a group of structural abnormalities of 1 or more layers of medium-sized and larger arteries that result in luminal narrowing…with or without associated aneurysms and dissections of the media" (6). Indeed, the chapter recounts in detail the manifestations and complications identified decades or more earlier with only limited advances from the 1960s (7–10).

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In this issue of the *Journal*, Kadian-Dodov et al. (11) provide the latest report of the U.S. Registry for Fibromuscular Dysplasia (11). This overall series of papers, similar to those of the International Registry of Aortic Dissection, has changed the way the medical community views, understands, and treats patients with FMD. Moreover, the authors' work makes it clear that clinicians are seeing FMD far more commonly than previously recognized. The authors have described an alarmingly high rate of aneurysm and dissection (~42%) among patients with FMD, of whom approximately one-third underwent a therapeutic intervention. Arterial dissection most commonly occurs in the extracranial carotid and vertebral arteries, with nearly 40% of these patients developing a dissection in more than 1 cervical artery. Importantly, 21% of the family members of patients with dissection had experienced sudden death. The authors also found a stroke rate of 29.2% in first- and second-degree family members. These data suggest a more lethal disease than previously understood.

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The current article complements previous publications by this group. Kadian-Dodov et al. (11) distinguished between the presentation in adults and that in children, described the current use of medical therapies, made clear the differences in presentation by patient sex, described the range of vessels commonly affected by the disease, brought forth new manifestations, like tinnitus, the carotid artery S-shaped curve, and coronary artery dissection, and created a new nomenclature to better define the disease (12–16). In contrast to the previous 50 years, this group has dramatically changed the way we think of FMD, showed that it may be much more common than previously recognized, and provided a platform for the study of the condition.

In addition to the specific FMD manifestations described in this paper, the authors have reinforced the importance of registries and patient involvement to enhance our knowledge of poorly understood "we see this" observations. As we have discussed previously (17), registry science is an important avenue to create mechanisms to improve the understanding of orphan or low-frequency diseases. Registries have become commonplace in cardiovascular medicine for the study of prevalent diseases, such as coronary artery disease, stroke, and peripheral artery disease. Many registries include information for disease presentation and management and often are used to extend the observations of clinical trials, to measure the use of indicated treatments, and to provide additional outcome data to inform the specifics of clinical practice.

The U.S. FMD registry is an excellent example of collaboration between patients and physicians. In our opinion, this model provides important opportunities to acquire new information and enhance understanding of poorly appreciated diseases. The patient-physician partnership can be synergistic and can markedly increase the pace of discovery. The patient component of the partnership brings additional strengths: the Fibromuscular Dysplasia Society of America (FMDSA) is a public health charitable organization that brings together patients with the disease. It coordinates support groups and disseminates information to patients across the nation. Importantly, the FMDSA can inform the collection of data based on personal experience. Moreover, FMDSA participants promote funding to support research and other activities through crowd sourcing and additional avenues typically unavailable to scientists and health care providers. Patients also bring energy and insight to complement the scientific endeavor of clinicians and researchers. Beginning these efforts with a broad-based interested coalition can minimize the time to first data collection.

Development of these registries also will enable research of the genetic underpinnings of these disorders with unusual phenotypes. FMD, like other diseases, has heterogeneous presentations and likely a significant asymptomatic component (18). As patients and families are accumulated and the disease phenotype clarifies, the opportunity to perform testing among various presentations will more rapidly uncover the genetic underpinnings of the disease. Some of this work has begun already (19).

Kadian-Dodov et al. (11) have contributed importantly to the evolution in our understanding of fibromuscular dysplasia and have demonstrated the power of collaborative physician-patient investigation. These efforts should serve as a model for patients and clinicians looking to advance the state of knowledge for problems currently underserved by the medical community.

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