EDITORIAL

New guidelines for rare cancer syndromes

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Many clinicians will encounter a given rare condition only a few times in their career. This makes management guidelines even more important—since personal clinical experience cannot guide clinical care. In this issue, ERN Genturis provides 2 guidelines for rare cancer syndromes [1, 2]. The guideline for Birt-Hogg-Dube defines clinical scenarios in which FLCN gene testing should be considered—including renal carcinomas, skin manifestations and pneumothorax [1]. Guidelines for renal cancer surveillance are also provided. ERN Genturis also provides guidelines on constitutional mismatch repair deficiency [2]. The guideline identifies scenarios in which genetic testing for this rare cancer predisposition syndrome should be considered and cancer surveillance recommendations. Genomic testing is central to the diagnosis of many cancer predisposition syndromes. Fortuno et al. report that many variants of uncertain significance in breast cancer predisposition genes could be reclassified as clinically actionable if variant reclassification is practiced [3]. Ancestry plays a key role in the spectrum of causal genetic variants encountered in given clinical scenarios—Kerr et al. report 2 highly prevalent BRCA variants in Orkney and Shetland islanders [4].

In this issue, novel genetic causes of rare conditions are also characterised. Mol et al. identify further people with connective tissue phenotypes and EFEMP1 gene variants [5]. The clinical presentation was notable for marfanoid body habitus and multiple herniae. Braddock et al. report autosomal dominant missense variants in SPARCL1 as a novel cause of corneal dystrophy [6]. SPARCL1 is known to regulate Decorin, which is a validated genetic cause of corneal dystrophy. Karimi et al. define the clinical spectrum of DEGCAGS (Developmental Delay with Gastrointestinal, Cardiovascular, Genitourinary, and Skeletal Abnormalities syndrome), which will aid clinical recognition and publish a diagnostic episignature [7]. A brief report in this issue also confirms the association of SOX11 variants with hypogonadotropic hypogonadism [8]. Autism is generally a multifactorial condition, but there are monogenic causes. Using exome and microarray analysis, Miyake et al. identified a monogenic cause in 16% of people with autism [9]. Some rare genetic conditions are treatable. Charpié et al. provide evidence that bisphosphonate therapy can reduce fracture risk in rare forms of osteogenesis imperfecta [10].

Discussing the benefits and limitations of genomic testing is crucial before people undergo diagnostic tests. Traditionally genetic counselling and testing occurred in specialist genetics clinics. Modern healthcare systems are removing this boundary and "mainstreaming" genomics testing in non-specialist clinics. Do et al. report a study of genetic counsellors views on mainstreaming genomic testing [11]. Genetic counsellors play a crucial role in supporting families with rare conditions. Wilsnack et al. report a mixed methods study of the support needs of families affected by telomere biology disorders, which highlights areas of focus for clinical care [12].

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AUTHOR CONTRIBUTIONS

AM conceived and wrote this paper.

COMPETING INTERESTS

The author declares no competing interests.