Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

also known as RIDDLIN, was implicated in association with RIDDLE Syndrome. *RNF168* encodes an E3 ubiquitin ligase protein involved in DNA double-strand break (DSB) repair.

Case presentation: Here described is an 11 year old girl who had her initial Genetics consultation at age 10 weeks due to poor weight gain with markedly decreased subcutaneous fat, bilateral talipes equinovarus deformity, abnormal liver function tests, dysmorphic features and a concern for parental consanguinity. Prenatal care was limited. SNP microarray analysis noted normal dosage but detected long contiguous regions of homozygosity (ROH) in multiple chromosomes, covering about 466.8 megabases. This was suggestive of apparent common descent, consistent with possible father-daughter parentage. This raised the suspicion for an autosomal recessive condition and detailed review noted that the *ERCC8* gene was encompassed in the ROHs reported and Cockayne Syndrome seemed to be a plausible diagnosis. However, *ERCC8* sequencing was normal.

Her brain MRI at age 2 months was unremarkable except for mild thinning of the corpus callosum, however, repeat imaging at about age 2 years was suggestive of focal cortical dysplasia type II in the posterior right frontal lobe. Additional findings noted during subsequently include epileptic encephalopathy, non-verbal autism spectrum disorder, ptosis, hypermetropia, cortical visual impairment, filum lipoma which was surgically released, bilateral vesicoureteral reflux and aberrant right subclavian artery. Exome Sequencing was recommended but not feasible due to insurance constraints, in spite of multiple authorization attempts. Facial recognition technology was also used as an aid but suggested diagnoses that were either ruled out on microarray analysis or deemed highly unlikely. Insurance approval was secured for an Autism/Intellectual Disability Panel which detected a homozygous likely pathogenic variant in *RNF168*, well as a compound heterozygous variants in *TUBGCP6*, one of which was likely pathogenic and the other, a variant of uncertain significance. It was interesting to note that neither gene is located within the ROHs reported on microarray analysis.

Conclusion: Biallelic variants in *TUBGCP6* have been reported in association with autosomal recessive microcephaly and chorioretinopathy. Some individuals have intellectual disability and the majority have marked growth failure consistent with primordial dwarfism. Structural brain abnormalities described include simplified gyri, pachygyria and cerebellar vermian hypoplasia. Congenital heart defects, triphalangeal thumbs, cataracts and hypertonia have been reported rarely. It does not seem farfetched that this could be an additional diagnosis, however, the clinical significance of one of the *TUBGCP6* variants still remains unclear.

The confirmed diagnosis of RIDDLE Syndrome, although unexpected, was impactful because she had multiple X-rays in the past and this was an indication to limit her radiation exposure moving forward. She has had Immunology follow-up and was diagnosed with IgA deficiency with poor polysaccharide response. In keeping with her convoluted clinical course, she was found to have aortic dilation with no clear etiology. An aortopathy panel was therefore recommended and found to be non-diagnostic, detecting a heterozygous variant of uncertain significance in the *SLC2A10* gene, associated with autosomal recessive arterial tortuosity syndrome.

For the most part, her genotype seems to fit with her phenotype, however, the lingering riddle is whether or not there may be yet an additional diagnosis, given the degree of parental consanguinity, or that the clinical spectrum of RNF168-related disorder may actually be broader than recognized.

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Ophthalmology genetics clinic in the times of COVID-19: A hybrid model

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Background: Multidisciplinary clinics are common in clinical genetics practice, as they allow the expertise of multiple providers within a single visit and enable improved coordination of care and patient experiences. Our team initiated a combined Ophthalmology Genetics clinic during the COVID-19 pandemic, requiring creativity to enable appropriate social distancing in the context of spatial constraints. The goal of this clinic is to provide comprehensive ophthalmologic and genetics care for individuals with both syndromic and nonsyndromic ocular differences.

Case presentation: The clinic began in July 2020. Our institution had imposed work room personnel limitations to allow social distancing to prevent the spread of COVID-19. As a result, our clinic model involved a hybrid approach. Patients were first evaluated by the pediatric ophthalmologist (in clinic) to enable a thorough examination and discussion of ocular findings. The pediatric geneticist and genetic counselor (with trainees, if present) were then incorporated in the visit via Zoom, with an iPad in the patient exam room. The pediatric ophthalmologist summarized findings with the family and genetics team. The genetics team then reviewed medical and family history, and physical exam was in part visual inspection by the geneticist as well as in-person examination by the ophthalmologist. Testing strategies were then discussed and counseling provided.

The clinic has met on average one per month, and thus far 32 patients have undergone evaluation. Referrals have come from both inside and outside of the institution. Referrals to both genetics and ophthalmology are reviewed and appropriate patients routed to the multidisciplinary clinic. The most common reasons for referral have included congenital cataracts (n=6), anterior segment dysgenesis (n= 5), coloboma (n=2), megalocornea (n=2), and microphthalmia (n=2). Testing strategies have varied based on reason for referral, including chromosomal microarrays, single gene testing, gene panels, and exome sequencing.

Conclusion: The hybrid model has served the clinic well to date. It allows for communication between providers during the visit and in a transparent manner, as the patient/family is present during this communication. It has also enabled all providers to be "present" simultaneously, which would otherwise be discouraged for social distancing purposes. The multidisciplinary model allows for more accurate ocular phenotyping to inform the genetic testing approach. While dysmorphology examination by the geneticist is somewhat limited through the video, it is supplemented by the in-person evaluation of the ophthalmologist. The hybrid clinic model could also be useful in future implementation of multidisciplinary clinics across different campuses or sites as well. Further research is needed to assess patient experiences.

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