4th International Conference on Pediatrics and Neonatal Care

July 23-24, 2025 | Paris, France

Maud Favier[1,2]; Elise Brischoux-Boucher[1]; Louise C. Pyle[3]; Nicolas Mottet[4]; Marion Auber-Lenoir[5]; Julie Cattin[4]; Eric Dahlen[6]; Christelle Cabrol[1]; Francine Arbez-Gindre[7]; Tania Attié-Bitach[8,9]; Odile Boute[10]; Louise Devisme[10]; Detlef Trost[11]; Aicha Boughalem[11]; David Chitayat[12]; Lev Prasov[13,14]; Odelia Chorin[15]; Annick Rein-Rothschild[15,16]; Eran Kassif[16,17]; Tal Weissbach[16,17]; Laura Godfrey Hendon[18]; Margaret P. Adam[19]; Chloé Quelin[2,20]; Sylvie Jaillard[21]; Laura Mary[21]; Sietse M. Aukema[22]; Malou Heijligers[23]; Christine de Die-Smulders[23]; Sander Stegmann[23]; Lauren Badalato[24]; Adi Ben-Yehuda[25]; Claire Beneteau[2,26]; Pierre-Louis Forey[27]; Paul Kuentz[6,28]; Juliette Piard[1,28].

[1]Centre de Génétique Humaine, Centre Hospitalier Universitaire de Besançon, Université de Franche-Comté, Besançon, France. [2]SoFFoet - Société Française de Foetopathologie, Paris, France. [3]Division of Human Genetics, Department of Pediatrics, Children's Hospital of Philadelphia, Philadelphia, Pennsylvania, USA. [4]Département d'Obstétrique et de Gynécologie, Centre Hospitalier Universitaire de Besançon, Université de Franche-Comté, Besançon, France. [5]Département de Radiologie, Imagerie pédiatrique, prénatale et sénologie, Centre Hospitalier Universitaire de Besançon, Université de Franche-Comté, Besançon, France. [6]Université de Franche-Comté, Centre Hospitalier Universitaire de Besançon, Oncobiologie Génétique Bioinformatique, FHU-TRANSLAD et Institut GIMI, Besançon, France. [7]Anatomie et cytologie pathologiques, Foetopathologie, Centre Hospitalier Universitaire de Besançon, Université de Franche-Comté, Besançon, France. [8]Laboratoire de biologie médicale multisites SeqOIA, Assistance Publique Hôpitaux de Paris, Paris, France. [9]Institut Imagine, INSERM U1163, Université Paris Descartes, Paris, France. [10]Pôle de Biologie Pathologie Génétique, Centre Hospitalier Universitaire de Lille, Lille, France. [11]Génétique et Cytogénétique, Laboratoire Cerba, Saint-Ouen l'Aumône, Paris, France. [12]Mount Sinai Hospital, University of Toronto, Toronto, Canada. [13]Department of Ophthalmology and Visual Sciences, W.K. Kellogg Eye Center, University of Michigan, Ann Arbor, Michigan, USA

ISBN: 978-1-917892-12-4

http://doi.org/10.51219/URForum.2025.Maud-Favier

[14]Department of Human Genetics, University of Michigan, Ann Arbor, Michigan, USA. [15]Institute of Rare Diseases, Edmond and Lily Safra Children's Hospital, Sheba Medical Center, Tel-Hashomer, Israel. [16]School of Medicine, Faculty of Medical and Health Sciences, Tel-Aviv University, Tel-Aviv, Israel. [17]Department of Obstetrics and Gynecology, Sheba Medical Center, Tel Hashomer, Israel. [18]Mississippi Medical Center, Jackson, Mississippi, USA | [19]Division of Genetic Medicine, Seattle Children's Hospital, Seattle, Washington, USA[20]. Service de génétique clinique, Centre Hospitalier Universitaire de Rennes, Université de Rennes, Rennes, France[21]. Service de Cytogénétique et Biologie Cellulaire, Centre Hospitalier Universitaire de Rennes, Université de Rennes, Rennes, France[22]. Department of Medical Genetics, Carl von Ossietzky University, Oldenburg, Germany[23]. Department of Clinical Genetics, Maastricht University Medical Centre, Maastricht, The Netherlands[24]. Department of Pediatrics, Kingstone General Hospital, Queen's University, Kingston, Canada[25]. Medical Genetics Institute, Shaare Zedek Medical Center, Jerusalem, Israel[26]. Service de Génétique Médicale, Centre Hospitalier Universitaire de Bordeaux, Université de Bordeaux, Bordeaux, France[27]. Département d'Obstétrique et de Gynécologie, Centre Hospitalier Universitaire de Grenoble, Université de Grenoble, Grenoble, France[28]. Université de Bourgogne, INSERM UMR1231 GAD “Génétique des Anomalies du Développement”, Dijon, France.

Fetal Presentation of MYRF-Related Cardiac Urogenital Syndrome: An Emerging and Challenging Prenatal Diagnosis

Purpose

MYRF-related cardiac-urogenital syndrome (MYRF-CUGS) is a rare condition associated with heterozygous MYRF variants. The description of MYRF-CUGS phenotype is mostly based on postnatal cases and 36 affected individuals have been published so far. We aim now to delineate the prenatal phenotype of MYRF-CUGS by reporting clinical data from fetuses and neonates with a pathogenic MYRF variant.

Methods

Detailed radiographic, pathological, clinical, and molecular data from 12 prenatal cases were collected through an international collaborative study. Adding the five fetuses previously published, we were able to study a cohort of 17 cases.

ISBN: 978-1-917892-12-4

http://doi.org/10.51219/URForum.2025.Maud-Favier

Results

Main ultrasound-accessible manifestations of MYRF-CUGS include congenital heart defects (CHD) (13/17, 76%), congenital diaphragmatic hernia (CDH) (10/17, 59%) and disorders of sexual differentiation (DSD) in 46, XY fetuses (7/14; 50%). Postnatal examination and/or autopsy data highlighted additional birth defects and neurological findings with a large spectrum of severity. In total, including pre- and early post-natal findings, we confirmed fetal clinical expression of MYRF-CUGS with a recurrent malformative association, including CHD (15/17, 88%), CDH (12/17, 71%), pulmonary hypoplasia (10/17, 59%) and DSD in 46, XY fetuses (11/14, 79%). The risk of associated developmental delay and intellectual disability (DD/ID) appear to be high (75%, 3/4 living cases from our cohort) and consistent with percentages reported in the literature in postnatal cohorts. Although MYRF is known to be involved in the fetal and early post-birth ocular development, the reproducibility of a prenatal nanophthalmos phenotype needs more investigation. We reported five news inherited cases with extreme intrafamilial variable expressivity. Molecular results revealed ten previously unpublished variants, one missense and nine predicted truncating variants (three frameshift, three nonsense and three splice site variants). Phenotype-genotype correlations were unclear and syndromic MYRF-CUGS seems to be linked to MYRF haploinsufficiency.

Conclusion

We report the first prenatal cohort of MYRF-CUGS, allowing us to further characterize the variable expressivity of this rare disorder in fetuses. Severe congenital anomalies with a poor prognosis are more frequent than previously described in postnatal cases. Our data suggest that MYRF-CUGS is characterized by a recurrent recognizable malformative association, accessible to prenatal diagnosis, with a significant intrafamilial phenotypic variability making genetic counseling challenging.

ISBN: 978-1-917892-12-4

http://doi.org/10.51219/URForum.2025.Maud-Favier