

PRECISION MEDICINE IN PERINATAL CARDIOLOGY. SINGLE CENTER EXPERIENCE

Muñoz H¹, Enriquez G¹, Cortez F¹, Germain A¹, Triantafilo J¹, De la Jara C,¹ Perez AL¹, Enriquez R¹, Robert JA¹, Palermo M²
1. Obstetrics and Gynecology, Clinica las Condes, Santiago, Chile. 2. DIAGNOMED. Buenos Aires, Argentina

Objectives: Our objective is to describe use of precision medicine for diagnosis or rule out, cases of congenital heart disease (CHD) associated with single gene diseases or deletions (SGD).

Methods: We design a descriptive retrospective study. We reviewed the neonatology and Rare disease Center database of Clinica las Condes between January 2015 and march 2025. Patients with CHD and SGD or microdeletion (MD) were selected. SGD was identified using MLPA, gene panel or Exome analysis, from samples of amniotic fluid, or neonatal Blood. In each of the cases, type of CHD, SGD, molecular biology technique used, and the perinatal results are described.

Results: During the period 2015 to 2025, 30 cases of CHD associated with SGD were found. **80 % (24/30)** were diagnostic (abnormal fetus) and 20 % (6/30) to rule out SGD or healthy carrier (normal Fetus). In diagnostic group 58,3 % (14/24) was perform during prenatal period, and 41,7 % (10/24) postnatally.

In diagnostic group (24), 17 were SGD, 3 negative SGD and 4 ongoing. Rasopaties were most frequently gen diseases 35,3 % (6/17). The most common CHD were Rhabmyoma (5), Hypertrophic Myocardopathy (HT MCP) (4), and Double outlet Right Ventricle (4), Figures 1-3.

In abnormal fetus group with SGD (17), 5 IU Death or termination, 12 born alive. Of those, 8 died during the first year of life. Perinatal mortality 76,5 % (13/17). In normal fetus group 33,3 % (2/6) was carrier of HT MCP, the others were healthy.(Table 1).

Table 1. Single gen or deletion, cardiac malformation and outcome

Single Gene Disease-Indication	n	Congenital Heart Disease	Outcome
Noonan Syndrome	2	Hypertrophic Myocardopathy	IUFD, NND
Cornelia de Lange	2	Double outlet Right Ventricle	2 Dies before 1 year
Costello Syndrome	2	Hypertrophic Myocardopathy	IUFD, NND
CHARGE	2	Double outlet Right Ventricle	TOP, Dies before 1 year
Kabuki Syndrome*	1	Single Ventricle	NND
Neurofibromatosis Type II	1	Cardiac insufficiency	Alive
6p - Syndrome	1	Aortic Arch Hypoplasia	TOP
4p - Syndrome	1	Cardiac insufficiency	TOP
Atrofia muscular espinal	1	Aortic Coartation	Dies before 1 year
5p - 7p+	1	Fallot	TOP
Rhabdomyoma Ts1, TS2	5	3 TS - 2 Ongoing	3 TS - 2 Ongoing
Hypertrophic MCP	2	Carrier, Ongoing	Carrier, Ongoing
Long Qt Syndrome Syndrome	3	2 Neg Healthy- 1 ongoing	2 Healthy- 1 ongoing
1 t hydropericardium	1	Neg RV Diverticulum	RV Diverticulum
Isomerism	1	Neg- Isomerism	Isomerism
SHVI	1	Neg - HLHS	HLHS
Hidrops 1 t NIPT normal	3	Neg, XO Mosaicism, Than Dys	TOP, 2 Ongoing
sister NF1, SETBP1	1	Neg Healthy	Alive

Hypertrophic CM: Hypertrophic Cardiomyopathy. DORV: double outlet right ventricle. HLHS: Hypoplastic left heart Syndrome. IUFD: intrauterine fetal death; TOP: termination of pregnancy; NND: neonatal death. Than Dys: Thanatophoric Dysplasia

Conclusion: Precision medicine has made it possible to identify the cause in about 15% of CHD. Our results show 85% of positive results (SGD/MD). in patients with CHD family history, or CHD associated to SGD. In high risk CHD patients, SGD study, make it possible for parents and the perinatal cardiology team to decide to continue the pregnancy, limit the therapeutic effort in the newborn, identify or rule out SGD in healthy fetuses in carrier mothers. Although SGD fetuses have a mortality rate of 68,4 % (13/19) of cases, in a short time gene or replacement therapy will significantly improve the survival of patients with CHD and SGD.

Figure 1. Rhabdomyioma

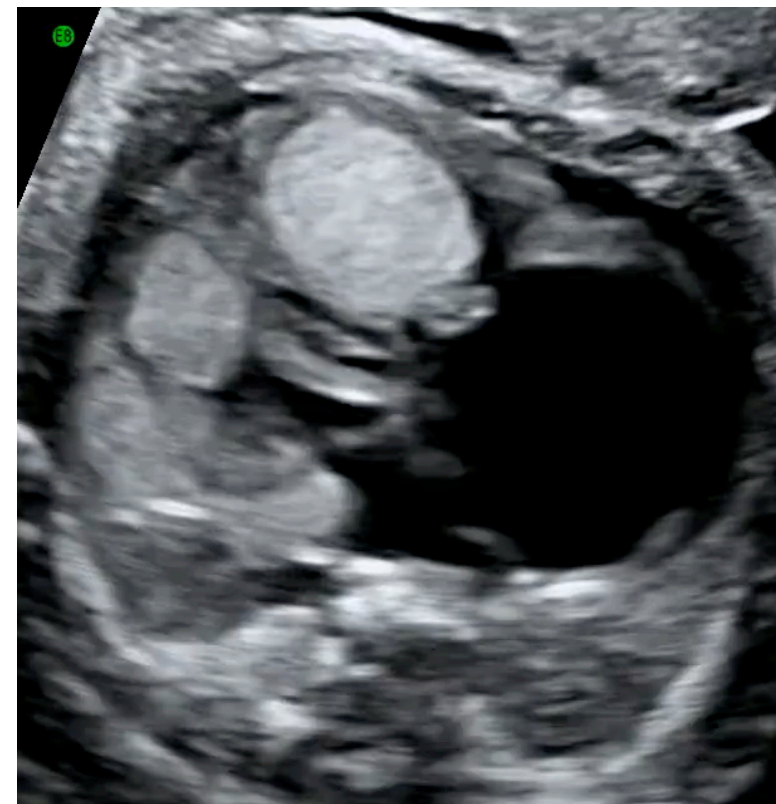


Figure 2. Hypertrophic CM



Figure 3. DORV

