Recognizing the clinical phenotypes of Cornelia de Lange Syndrome a case report

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Abstract

The wide range of genetic diseases usually have clinical manifestations at a structural and neurodevelopment level, this also apply to the Cornelia de Lange syndrome which is associated to divers errors on the genetic structures of NIPBL,SMC1A, SMC3, RAD21, HDAC8. This genes regulate cohesin which takes an important rol in chromatin fusion. The Cornelia de lange syndrome has different phenotypic characteristics clinically speaking, including growth restriction, variable cognitive deficit, upper extremity malformations and distinct characteristics on cranial bone and face which can help to make an early clinical diagnostic [1]. Here a 2 month old girl is presented who had a low weight at birth of 1320 gr and various phenotypic craneofacial and extremity malformations compatible with cornelia de lange syndrome.

Key words: Cornelia de Lange Syndrome, Synophrys, Dismorphism

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Introduction

We describe a 2-month-old baby girl, the second child to a nonconsanguineous couple from Honduras.

At her birth, the mother was 31 years old with no history of teratogenic exposures and no comobirdities before or during pregnancy.

At birth with intrauterine growth restriction and very low weight of 1320 gr (<3 percentile), length 36 cm (<3 percentile), with microcephaly with an OFC of 27.5 cm (<3 percentile).

Case

At physical examination with synophrys, generalized hypertricosis and depressed nasal bridge, upper limb meromelia (Figure 1) and cutis marmorata (figure 2).

At birth she was hospitalized like Cornelia de Lange Syndrome because of her clinical characteristics and it was found left cystic kidney, left ureteral stenosis, ependemmary cyst and a ventricular septal defect [2].

Unfortunately we do not have a genetical evaluation but the clinical findings can orient any physician to make the diagnosis.

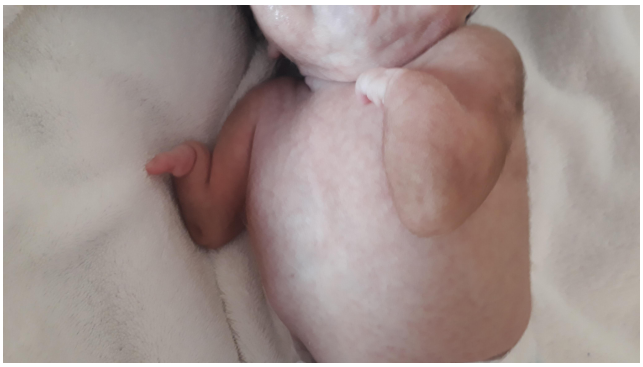

Figure1: Cleft palate, upper limb meromelia.

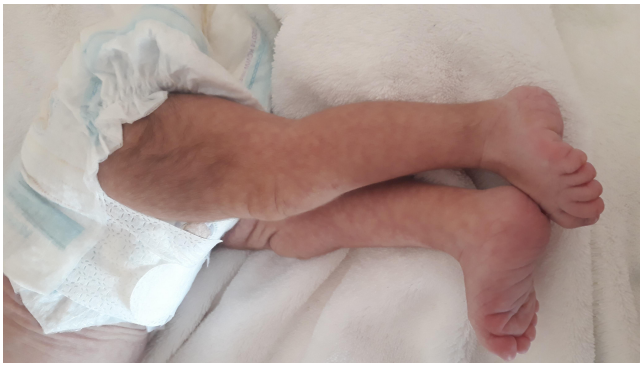

Figure2: Cutis marmorata.

Discussion

Cornelia de Lange Syndrome is a dominantly inherited disorder characterized by abnormalities in the upper limbs, hirsutism, growth, and cognitive retardation. It is a heterogeneous disorder that shows a wide phenotypic range. The prevalence described is 0.5- 1/10.000 live births, in our research we found two clinical cases published in Honduras.

Clinical features

There are three phenotypes described by Gillis in 2004 with a wide spectrum. This classification is based in three physical characteristics: The level of limb reduction, the developmental and cognitive abilities and the growth percentile that can be from mild to severe affectation [3].

The syndrome has a broad spectrum from mild to severe clinical features, where almost every organ system can be affected. The most common involved are neurodevelopmental, craniofacial, gastrointestinal and musculoskeletal systems in Table 1 we describe the most common features by systems.

Table1: *Common clinical features in Cornelia de Lange Syndrome adapted of Sanz et al.*

Craniofacial Features	Microcephaly
	Low hair implantation
	Low ear implantation
	Synophrys
	Long eyelashes
	Anteverted nostrils
	Fine lips
	Elongated filtrum
	Retromicrognathia
Growth and Nutrition	Intrauterine growth restriction
	Posnatal growth retardation
CNS	Cognitive delay
Musculoskeletal	Severes: Amelia, phocomelia, meromelia oligodactyly
	Mild: Clinodactily, sindactily, short fifth finger
others	Hypertrichosis
	Cutis marmorata 60%

Diagnosis

Phenotypically the classic Cornelia de Lange syndrome has clinical characteristics that make it easy to identify by qualified personnel, clinically it stands out for different craniofacial malformations accompanied by shortened upper extremities and with birth weight below the 5th percentile [4]. In 2018 a group of international experts, established an international Cornelia de Lange Syndrome Consensus group, they classified several features described as: 6 cardinal signs (2 pts each), 7 suggestive signs (1 pts each), whereas if the score is greater than or equal to 11, it is considered a classic phenotype, 9-10 is considered a non-classical phenotype, 4-8 of which 1 is a cardinal sign, genetic tests must be indicated, and less than 4 does not indicate genetic tests. Prenatal diagnosis have a greater degree of difficulty, with intrauterine growth failure being one of the main characteristics, where the literature reports cephalic and abdominal fetal circumference that falls below the 10th percentile, in the third trimester. In the ultrasound we can find an interesting tool, though it's findings will depend on the degree of severity with which Cornelia de Lange syndrome occurs, where the observational is usually clinodactyly, monodactyly or complete absence of the upper limb. The easy characteristics can be suggestive [5]. Other malformations can also be identified, such as: diaphragmatic hernia, heart disease.

Conclusion

There is no relationship between alterations in amniotic fluid volume and Cornelia de Lange syndrome. For the right therapeutic guideline, interdisciplinary attention is required with otorhinolaryngologists, neurologists, psychology, gastroenterologist, and surgery, which must annually monitor psychomotor development. Growth and assess heart and kidney function.

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