REVISTA ECUATORIANA DE PEDITRÍA
rev-sep.ec

CLINICAL CASE

Severe right ventricular hypertrophy secondary to pulmonary valve stenosis in an older infant with Noonan syndrome: a case report

David Reinoso [ID] [1] * , Ana Pazmino [ID] [2], Raul Rios [ID] [3]

1. Postgraduate in Cardiology, Pontificia Universidad Católica del Ecuador, Quito, Ecuador.
2. Postgraduate in Pediatrics, University de las Américas, Quito, Ecuador.
3. Child Cardiovascular Intervention Service, Baca Ortiz Pediatric Hospital, Ministry of Health, Quito, Ecuador.

Received: January 4, 2023
Accepted: March 27, 2023
Published: April 26, 2023
Editor: Dr. Francisco Xavier Jijón Letort.

Bibliographic letterhead:
Reinoso D, Pazmino A, Rios R. Severe right ventricular hypertrophy secondary to pulmonary valve stenosis in an older infant with Noonan syndrome: A case report. Revista Ecuatoriana de Peditría 2023;24(1):16-23. DOI:https://doi.org/10.52011/187
ECUADORIAN SOCIETY OF PEDIATRICS
e-ISSN: 2737-6494

Abstract

Introduction: Noonan syndrome is characterized by growth disorders, psychomotor and mental retardation, facial dysmorphia, musculoskeletal disorders, and cardiac disorders in up to 80% of patients, hypertrophic cardiomyopathy in 30%, pulmonary valve stenosis in 50%, septal defects, pulmonary branch stenosis, tetralogy of Fallot, and aortic coarctations.

Clinical case: 8-month-old infant with hypertelorism, palpebral ptosis, low-set ears, short neck, and scoliosis. It presents with cyanosis and dyspnea associated with muscle hypotonia. Weight: Z score: -3, height: Z score: -3, on cardiac auscultation: mid-systolic murmur grade 4/6 in the second left intercostal space, parasternal line. The echocardiogram shows moderate valvular pulmonary stenosis (52 mmHg systolic gradient) and dilatation of the pulmonary arterial trunk.

Evolution: Cardiac catheterization was performed with evidence of severe pulmonary valve stenosis, infundibular reaction, right ventricular hypertrophy, dome valve opening, and "type E" filiform patent ductus arteriosus. These findings justified the development of cardiac hypertrophy. Pulmonary balloon valvuloplasty was performed, which improved cardiac pressure.

Conclusions: The cardiac alterations present in an infant with Noonan syndrome were biventricular hypertrophy, pulmonary hypertension, pulmonary valve stenosis, and patent ductus arteriosus.

Keywords: MESH: Noonan syndrome, Right ventricular hypertrophy, Right ventricular outflow obstruction, Pulmonary valve stenosis.

Introduction

Noonan syndrome is a multisystem genetic disorder occurring in 1 in 2,500 live newborns caused by a mutation of the PTPN11 gene [1, 2]. It is a known but largely

* Corresponding author.

Email: < davidirr89.dr@gmail.com > David Reinoso Recalde/Address: Ave 12 de Octubre 1076, Quito 170143. Telephone: [593] 02 2991700

underdiagnosed autosomal dominant disease since its clinical manifestations in some patients show abundant signs and symptoms and in others only some discrete characteristics [3].

It is mainly associated with failure to thrive and congenital heart disease, especially pulmonary valve stenosis [2]. It must be considered that he may have secondary heart disease, dysmorphic facial features, psychomotor retardation, and skeletal abnormalities, among others [1, 2].

The discovery of the molecular genetic causes of Noonan syndrome and Noonan syndrome-related disorders has allowed us to better understand the mechanisms underlying the different symptoms of these diseases and to establish genotype-phenotype correlations (in growth patterns, for example). In addition to the classic clinical features of Noonan syndrome, critical new features include decreased fertility in males, a lean phenotype with increased energy expenditure and a possible impact on carbohydrate metabolism/insulin sensitivity, and impaired bone health. Further clinical studies are needed to investigate the long-term implications of these findings and their potential interconnections [4].

Clinical case

Clinical history

Breastfeeding patients under eight months of age with the following personal history:

- Prenatal: Product of the sixth pregnancy of a 36-year-old mother (elderly mother) with a history of 4 repeated spontaneous abortions, last pregnancy (patient) with ultrasound report at the fourth month of cystic hygroma, umbilical cord study was performed, discarding trisomy 21.
- Natal: Born at 39 weeks by cesarean section due to fetal distress, anthropometric data within normal parameters.
- Postnatal: Admitted to neonatology due to respiratory distress that required invasive mechanical ventilation for 15 days. Gastrostomy was performed due to the absence of the sucking reflex and lack of weight gain with delayed psychomotor development.

During this admission, he was diagnosed with ventricular hypertrophy in a control electrocardiogram (Figure 1).

Physical exam

Physical exam: Facial: hypertelorism, ptosis, low-set ears, short neck. Dorsal region scoliosis is evident. Cyanosis and dyspnea associated with muscular hypotonia were evident. Weight: Z score: -3, height: Z score: -3. Cardiac auscultation: mid-systolic murmur grade 4/6 in the second left intercostal space, parasternal line, with irradiation toward the right hemithorax. Abdomen without visceromegaly, gastrostomy button. Genital region: nonpalpable testicles in the scrotum.

Complementary exams

Complete blood count with a regular report. Biochemistry: preserved renal function, total creatine phosphokinase 31.60 U/L, ultrasensitive troponin T 12.57 pg/ml, and 1-4 alpha glucosidase greater than 4.46 µmol/L/h. Hormonal: IGF1, insulin-like growth factor less than 15 ng/ml, luteinizing hormone less than 0.1 mU/ml, testosterone less than 2.5 ng/dl, hydrocortisone 17.52 ug/dl, TSH 1.71 mIU/L, free T3 3.37 nmol/L, free T4 1.27 nmol/L.

Echocardiogram showed moderate valvular pulmonary stenosis and dilatation of the pulmonary artery trunk (Figure 2). The 2-dimensional echocardiogram showed biventricular concentric hypertrophy with an ostium secundum interatrial septal defect. (Figure 3)

Figure 1. Electrocardiogram: sinus rhythm, heart rate 121 beats per minute, the electrical axis in extreme right, positive T wave in right precordial leads, and deep S wave in left precordial leads.

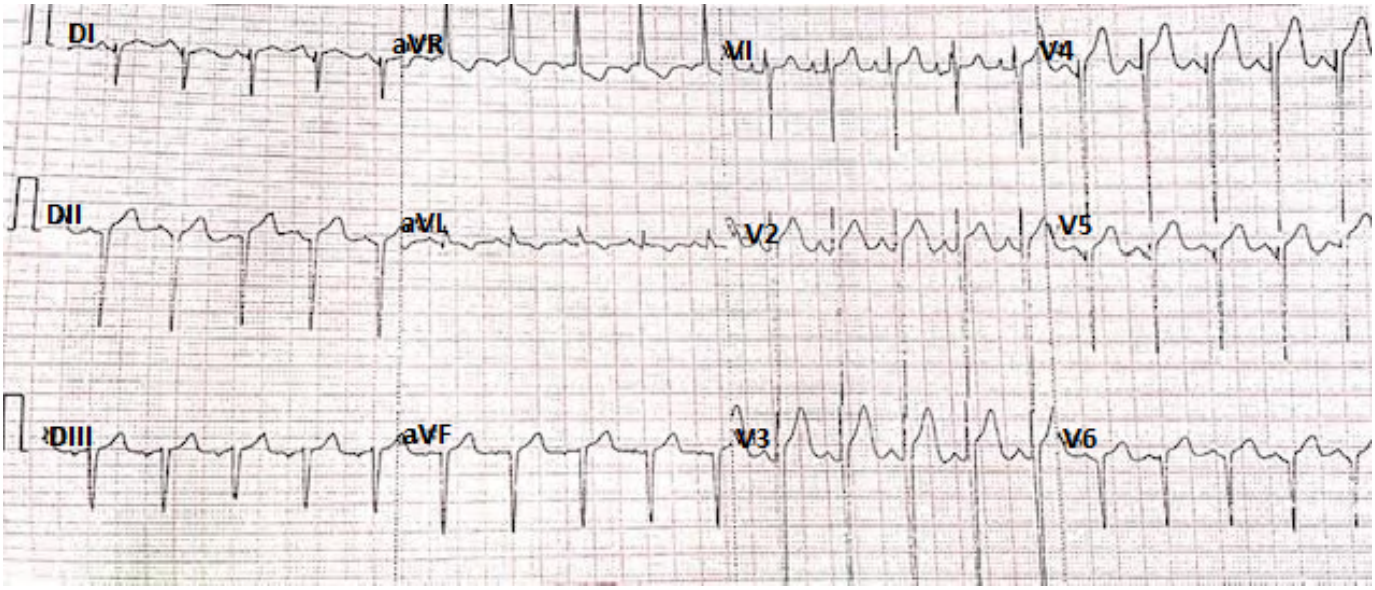
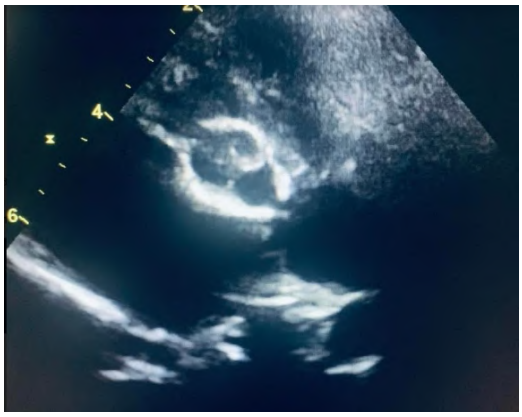


Figure 2. A. Two-dimensional echocardiography. B. Color Doppler: moderate-grade valvular pulmonary stenosis (systolic gradient of 52 mmHg) and dilatation of the pulmonary arterial trunk.



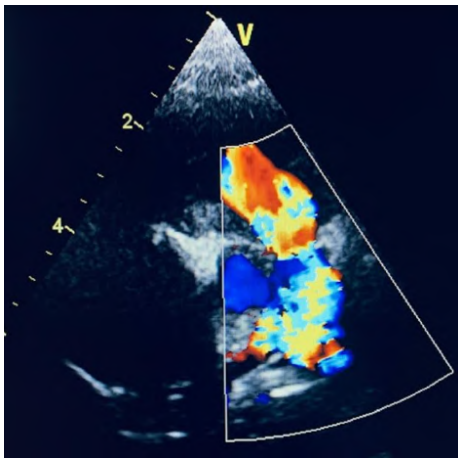


Figure 3. 2D echocardiography: Biventricular concentric hypertrophy (predominantly left). Interatrial septal defect ostium secundum: 4.5 mm in diameter.

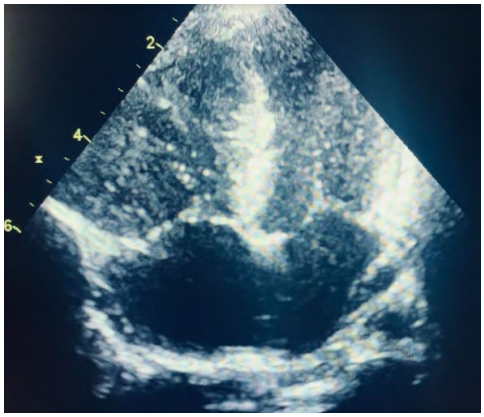


Figure 4. Angiography: "Type E" filiform patent ductus arteriosus.

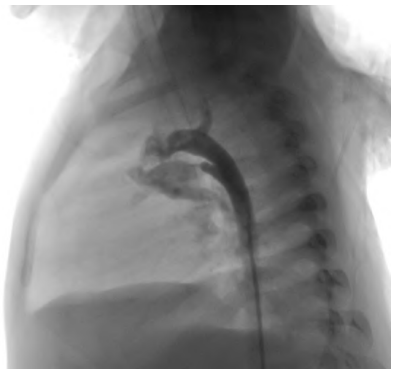


Figure 5. Lateral angiography prevalvuloplasty: A. Note infundibular reaction. B. Right ventricular hypertrophy and dome valve opening.

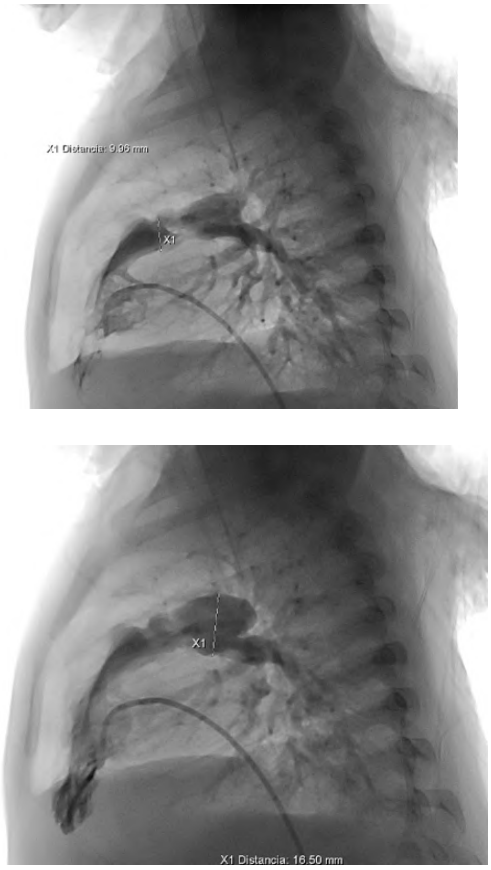
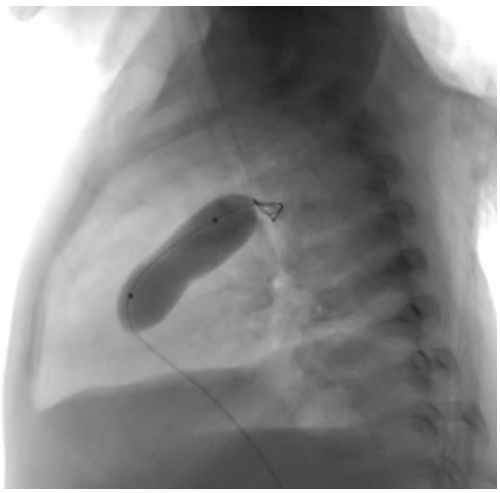


Figure 6. Left lateral angiography: Balloon pulmonary valvuloplasty; note the waist in the silhouette of the balloon as the stenotic valve is opened.



Skeletal muscle biopsy

Striated muscle fibers with slight interstitial edema, without cytoplasmic alterations that suggest substance deposition. Absent inflammatory infiltrate.

Evolution

The patient underwent cardiac catheterization, which revealed "type E" filiform patent ductus arteriosus (Figure 4), infundibular reaction, right ventricular hypertrophy, and dome valve opening (Figure 5). Pulmonary balloon valvuloplasty was performed (Figure 6), which improved cardiac pressure. After this intervention, he was discharged in stable condition, and external consultants carried out his follow-up.

Discussion

Noonan syndrome is a genetic disorder that causes multiple congenital disabilities. Most affected individuals have characteristic facial features, which evolve with age. Familial recurrence is consistent with an autosomal dominant mode of inheritance, but most cases are due to de novo mutations [4]. In the present case, an 8-month-old infant presented on physical examination with hypertelorism, ptosis of the eyelids, low-set ears, a short neck, and scoliosis. In addition, cyanosis and dyspnea associated with muscular hypotonia were observed. Weight: Z score: -3, height: Z score: -3, on cardiac auscultation: grade 4/6 mid-systolic murmur in the second left intercostal space, parasternal line, irradiating toward the right hemithorax. The echocardiogram shows moderate valvular pulmonary stenosis (52 mmHg systolic gradient) and dilatation of the pulmonary arterial trunk. It must be considered that cardiac alterations in this syndrome occur in up to 80% of patients with a higher frequency of pulmonary valve stenosis [5], as reported in this case.

The diagnosis of Noonan syndrome requires high clinical suspicion [6], which is why several scoring systems have been created to help determine it, such as the Van der Burg system used since 1994 [7].

Thus, the combination of features, including typical facial features, short stature, skeletal abnormalities, presence of cardiac defects, mild developmental delay, and cryptorchidism [8], are diagnostic features, as indicated in this patient.

Subsequently, a genetic analysis will be requested for confirmation [9].

After the complementary examinations were carried out, cardiac catheterization was carried out, and pulmonary valvuloplasty was performed with a balloon to improve the cardiac pressure.

Increased awareness of Noonan syndrome is proposed to reach an early diagnosis [10] so that patients suffering from it can obtain proper and early treatment. This patient could be the beneficiary of multidisciplinary treatment, managing to treat his valve disease and improve his condition and life prognosis.

Conclusions

Cardiac abnormalities present in an infant with Noonan syndrome were biventricular hypertrophy, pulmonary hypertension, pulmonary valve stenosis, and patent ductus arteriosus.

Abbreviations

Not declared.

Supplementary information

No supplementary materials are declared.

Acknowledgment

Not declared.

Author contributions

David Israel Reinoso Recalde: bibliographic review and writing of the manuscript
Ana María Pazmiño Miranda: review and critical analysis of the article
Raúl Ríos Méndez: case writing, a compilation of paraclinical examinations and biopsies.
All authors read and approved the final version of the manuscript.

Financing

The authors of this article financed the expenses of this research.
The health home financed hospital costs, and there were no additional expenses for the patient's guardians.

Availability of data and materials

Data were collected from medical files and are not publicly available due to participant confidentiality but are available through the corresponding author under clearly justified academic requests.

Statements

Ethics committee approval and consent to participate

Not required for clinical cases.

Publication Consent

The authors have the informed consent of the patient's mother for the publication of the clinical case, as well as for the images presented for academic purposes, safeguarding the confidentiality of the minor.

Conflicts of interest

The authors declare they have no conflicts of interest.

Author Information

Not declared.

References

1. Zenker M, Edouard T, Blair JC, Cappa M. Noonan syndrome: improving recognition and diagnosis. Arch Dis Child. 2022 Dec;107(12):1073-1078. doi: 10.1136/archdischild-2021-322858. Epub 2022 Mar 4. PMID: 35246453; PMCID: PMC9685729. https://doi.org/10. 1136/archdischild-2021-322858

2. Roberts AE, Allanson JE, Tartaglia M, Gelb BD. Noonan syndrome. Lancet. 2013 Jan 26;381(9863):333-42. doi: 10.1016/S0140-6736(12)61023-X. Epub 2013 Jan 10. PMID: 23312968; PMCID: PMC4267483. https://doi.org/10. 1016 / S0140-6736(12)61023-X

3. Romano AA, Allanson JE, Dahlgren J, Gelb BD, Hall B, Pierpont ME, Roberts AE, Robinson W, Takemoto CM, Noonan JA. Noonan syndrome: clinical features, diagnosis, and management guidelines. Pediatrics. 2010 Oct;126(4):746-59. doi: 10.1542/peds.2009-3207. Epub 2010 Sep 27. PMID : 20876176. https://doi.org/10.1542/peds.2009-3207

4. Yart A, Edouard T. Noonan syndrome: an update on growth and development. Curry Opin Endocrinol Diabetes Obes . 2018 Feb;25(1):67-73. doi: 10.1097/MED.0000000000000380. PMID : 29120925. https://doi.org/10.1097/MED.0000000000000380 _

5. Bhambhani V, Muenke M. Noonan syndrome. Am Family Physician. 2014 Jan 1;89(1):37-43. PMID: 24444506; PMCID: PMC4099190. https://pubmed.ncbi.nlm.nih.gov/24444506/

6. Chinton J, Huckstadt V, Moresco A, Gravina LP, Obregon MG. Clinical and molecular characterization of children with Noonan syndrome and other RASopathies in Argentina. Arch Argent Pediatric . 2019 Oct 1;117(5):330-337. English Spanish. doi: 10.5546/aap.2019.eng.330. PMID: 31560489.
https://doi.org/10. 5546 / aap.2019.eng.330

7. Carcavilla A, Suárez-Ortega L, Rodríguez Sánchez A, Gonzalez-Casado I, Ramón-Krauel M, Labarta JI, Quinteiro Gonzalez S, Riaño Galán I, Ezquieta Zubicaray B, López-Siguero JP. Noonan syndrome: genetic and clinical update and treatment options. An Pediatr (Engl Ed). 2020 Jul;93(1): 61.e 1-61.e14. English. doi: 10.1016/j.anpedi.2020.04.008. Epub 2020 May 31. PMID: 32493603 .
https://doi.org/10. 1016 / j.anpedi.2020.04.008

8. Turner AM. Noonan syndrome. J Pediatric Child Health. 2014 Oct;50(10):E 14-20. doi: 10.1111/j.1440-1754.2010. 01970.x. Epub 2011 Jul 19. PMID: 21771153.
https://doi.org/10. 1111 /j. 1440-1754.2020.01970.x.

9. Rodríguez F, Gaete X, Cassorla F. Etiology and Treatment of Growth Delay in Noonan Syndrome. Front Endocrinol (Lausanne). 2021 Jun 4;12:691240 . doi: 10.3389/fendo.2021.691240. PMID: 34149626; PMCID: PMC8212989.
https://doi.org/10. 3389 / fendo.2021.691240

10. van der Burgt I. Noonan syndrome. Orphanet J Rare Dis. 2007 Jan 14;2:4 . doi: 10.1186/1750-1172-2-4. PMID: 17222357; PMCID: PMC1781428.
https://doi.org/10. 1186/1750-1172-2-4

DOI: Digital Object Identifier. PMID: PubMed Identifier. SU: Short URL.

Editor's Note

The Revista Ecuatoriana de Pediatría remains neutral regarding jurisdictional claims on published maps and institutional affiliations.