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SMART PEDI UPDATE

Pedismart Newsletter
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Pedi smart News Letter
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Dear Doctor,
Greetings from Micro Labs Limited. We are happy to bring you **"PEDI SMART**"which contain latest and interesting news in the field of Paediatrics.

This issue contains:

1. **A study on the characteristics of children with co-occurring celiac disease and inflammatory bowel disease Seropositivity**
2. **A study comparing the obstetric and perinatal outcomes of singleton births after single- versus double-embryo transfer.**
3. **A retrospective cohort study on the local and systemic oxygen exposure in children with severe bronchiolitis receiving invasive mechanical ventilation**
4. **A case report of a 2-month-old infant with RIT1-associated Noonan syndrome and dilated coronary arteries.**

Should you require any specific article or medical information, please feel free to contact us at medicalservices@microlabs.in

Looking forward to your valuable feedback

Best Regards,

Medical Team, Micro Labs Limited

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1. A study on the characteristics of children with co-occurring celiac disease and inflammatory bowel disease Seropositivity

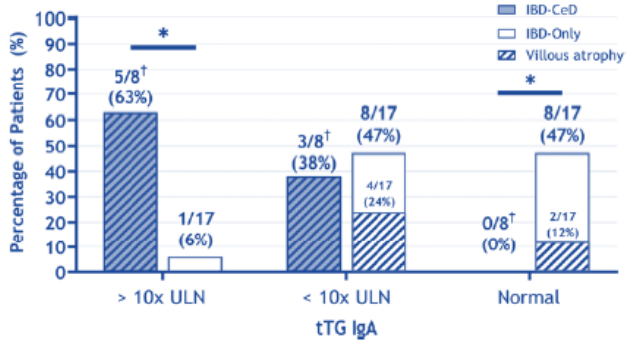
Introduction:

An autoimmune condition of the small intestine, celiac disease(CeD) is often referred to as gluten-sensitive enteropathy. The disorder known as celiac disease occurs when the body reacts improperly to gluten, resulting in inflammation and damage to the small intestine.[1] CeD is closely linked to various genetic disorders, co-occurring autoimmune diseases, and a family history of CeD in children. The diagnostic characteristics of CeD in patients with concomitant inflammatory bowel disease (IBD) are difficult to diagnose.There are currently few studies evaluating the coexistence of CeD and IBD in children. The objectives of this study were to describe the phenotypic of children who had IBD and were CeD seropositive and to assess how confident physicians were in their abilities to diagnose CeD in this population.

Due to a bidirectional relationship between celiac disease and inflammatory bowel disease (IBD), diagnosing celiac disease (CeD) in seropositive children

Methods:

Between 2006 and 2020, Researchers conducted a single-center retrospective cohort analysis of patients with IBD and CeD seropositivity who were under the age of 18. According to the guidelines of the North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition, subjects were considered to have IBD-CeD if their serology and histology results supported a diagnosis of CeD, and if their healthcare providers had CeD suspicions as determined by a survey. Seropositive subjects who did not match the criteria for CeD were included in the cohort limited to IBD. The Fisher exact test was used to evaluate demographic, histologic, gross endoscopic, and laboratory characteristics.



tTG IgA serology and villous atrophy in IBD-CeD and IBD-only (*$P < 0.05$). †Percentages may not total 100 due to rounding. CeD = celiac disease; IBD = inflammatory bowel disease; tTG = tissue transglutaminase.

Results:

When compared to 17 seropositive participants with IBD-only, 475 children with IBD had higher concomitant CeD, 5 had tissue transglutaminase (tTG) immunoglobulin A (IgA)

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levels greater than 10x upper limit of normal (ULN, P = 0.006), and 8 had villous atrophy (VA, P = 0.003). No children with IBD-CeD developed esophageal eosinophilia, duodenal cryptitis, duodenal ulceration, or fecal calprotectin >250 g/g. The absence of VA and intraepithelial lymphocytes, the presence of neutrophilic and eosinophilic duodenitis, diffuse ulceration, increased inflammatory markers, and immunosuppressive medication were all factors that made it difficult for physicians to diagnose CeD in patients with IBD.

Discussion:

Children with IBD and CeD seropositivity are discussed in this study, along with the characteristics that affected providers' confidence in diagnosing concurrent CeD. The probability of a CeD diagnosis was raised by high titers of tTG IgA and the presence of VA. IBD-CeD was not usually associated with esophageal eosinophilia, duodenal cryptitis, duodenal ulceration, thrombocytosis, or increased faecal calprotectin. Notably, the difficulty in detecting and treating comorbid CeD was worsened by immunosuppressive medication for IBD. Researchers gain a more sophisticated understanding of CeD diagnosis in IBD in this study.[3] Alper et al. found false-positive tTG IgA in 5 of 130 participants (3.8%) while researchers found 9 of 475 subjects (1.9%) with positive tTG IgA that did not match the criteria for CeD.[4]

Conclusion:

There is a limitation of literature describing the characteristics of children with IBD and CeD seropositivity. This study offers a framework for understanding the relationship between IBD and CeD seropositivity, which may potentially help predict CeD. Without evidence-based guidelines, diagnosing and managing CeD in children with IBD remains difficult.

References:

1. Posner EB, Haseeb M. Celiac Disease. 2022 Aug 8. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; Jan 2022
2. Cheung T, de Zoeten EF, Hoffenberg EJ, Liu E, Pan Z, Walker T, Stahl M. Characteristics of Children With Inflammatory Bowel Disease and Coexisting Celiac Disease Seropositivity. J Pediatr Gastroenterol Nutr. 2022 Dec 1;75(6):737-742.
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4. Alper, Rojas-Velasquez D, Pashankar DS. Prevalence of anti-tissue transglutaminase antibodies and celiac disease in children with inflammatory bowel disease. *J Pediatr Gastroenterol Nutr* 2018;66:934–6.

2. A study comparing the obstetric and perinatal outcomes of singleton births after single- versus double-embryo transfer.

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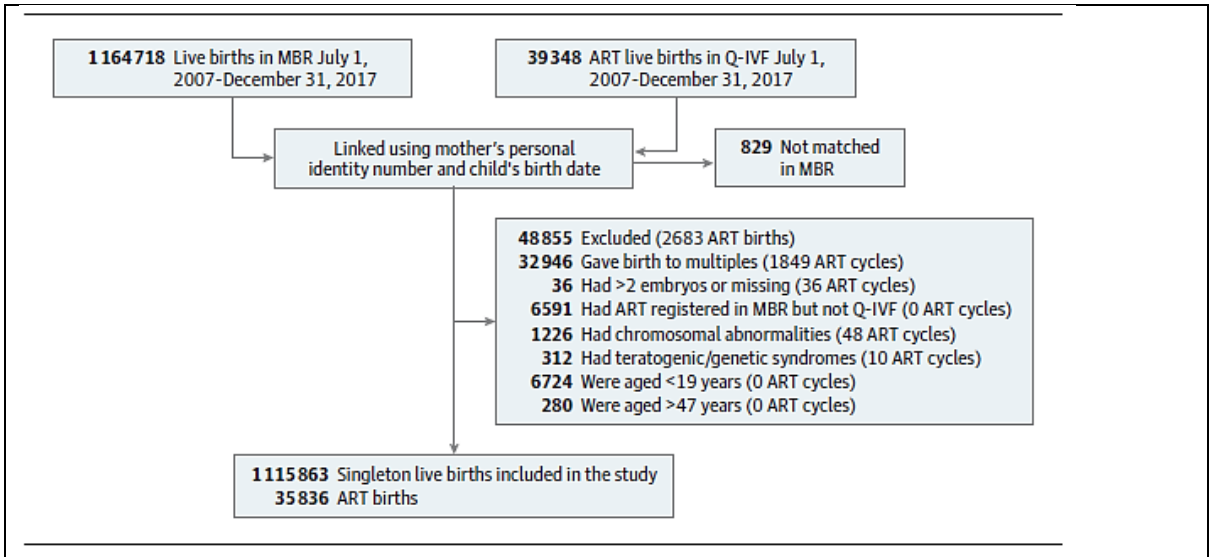
Introduction:

When compared to pregnancies that originate from natural conception, assisted reproductive technology pregnancies are associated with a higher risk of poor perinatal outcomes. Pregnancies brought on by the transfer of multiple embryos have been linked to these unfavorable outcomes.[1] Some countries impose restrictions on the number of transplanted embryos and actively encourage single-embryo transfer (SET), which effectively lowers high-risk twins or higher-order gestations, in order to improve the safety of assisted reproductive technology (ART) and reduce obstetric risks.[2] Double-embryo transfer (DET) is not only frequently requested by patients, but it is also more frequently performed in situations where the likelihood of pregnancy is reduced by old age, prior implantation failure, poor embryo quality, or other unfavorable circumstances. The probability of DET leading to multiple births is decreased by lower reproductive potential. As a result, many people undergoing DET are having a singleton pregnancy.[1] The purpose of this study is to compare the risk of adverse outcomes in singletons born via assisted reproduction employing single-embryo transfer (SET) and double-embryo transfer (DET).

Singletons born after Double-embryo transfer have a higher risk of negative outcomes than singletons born after single-embryo transfer.



Study Flow Diagram: ART indicates assisted reproductive technology; MBR, National Medical Birth Register; and Q-IVF, National Quality Registry for Assisted Reproduction.

Methods:

Data from women who delivered a singleton following SET or DET between 2007 and 2017 were used in this cohort analysis. These deliveries were recorded in the National Quality Registry for Assisted Reproduction. Researchers included all embryo transfers, whether they replaced cleavage or blastocyst-stage embryos in fresh or frozen treatment

cycles. Linking to the National Medical Birth Register enabled the retrieval of information on obstetric and neonatal outcomes. As a reference group, naturally conceived singletons were used. Between September 2021 and August 2022, data were examined. Exposures included a double embryo transfer that resulted in a singleton birth. In singleton births conceived with DET vs. SET, relative risk ratios or odds ratios (ORs) and absolute risk differences (ARDs) in percentage points with 95%CIs were determined for obstetric and perinatal outcomes.

Results:

A total of 30 713 singletons and 5123 singletons were born among the 1 115 863 births of singletons, respectively. After DET vs SET, singletons had a greater risk of infant death (OR, 2.67 [95%CI, 1.28-5.55]; ARD, 0.2 percentage points [95%CI, 0.0-0.4 percentage points]). DET was linked to a greater risk of low birth weight in frozen embryo transfers (OR, 1.64 [95%CI, 1.19-2.25]; ARD, 2.0 percentage points [95%CI, 0.5-3.5 percentage points]). DET was linked to very preterm delivery (relative risk ratio, 2.64 [95%CI, 1.50-4.63]; ARD, 1.8 percentage points [95%CI, 0.3-3.4 percentage points]) and lower birth weight (OR, 1.83 [95%CI, 1.29-2.60]; ARD, 3.2 percentage points [95%CI, 0.9-5.5 percentage points]) in blastocyst transfers.

Discussion:

In comparison to SET, researchers saw greater relative risks in this cohort of singletons born after DET for unfavourable infant health outcomes such neonatal death and significant congenital abnormalities. The absolute risks of these events were, however, low, and the ARDs were insignificant and minor.[1] When IVF and ICSI were compared to spontaneous conception, researchers were able to detect a minor tendency toward growth limitation, but the whole data set revealed no differences in birth weight for gestational age (BWGA) between DET and SET. Similar to earlier reports, the tendency for increased BWGA when frozen cycles were compared to fresh cycles was observed in this in this cohort .[3]

Conclusion:

These findings suggest that, compared to singletons born after SET, singletons born after DET are at a higher risk of negative outcomes. After DET using frozen embryos and blastocysts, negative results were mostly seen in singletons.

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2. Meldrum DR, Adashi EY, Garzo VG, et al. Prevention of in vitro fertilization twins should focus on maximizing single embryo transfer versus twins are an acceptable complication of in vitro fertilization. *Fertil Steril*. 2018;109(2):223-229

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3. A retrospective cohort study on the local and systemic oxygen exposure in children with severe bronchiolitis receiving invasive mechanical ventilation.

Introduction:

Bronchiolitis, an acute viral infection, is an inflammation of the bronchioles. In children under the age of two, it is the most frequent lower respiratory tract infection. It is now among the most frequent causes of hospitalisation in the winter for children under the age of two.[1] Despite being an usually mild condition, children with severe bronchiolitis who are admitted to the PICU often need invasive mechanical ventilation (IMV) to avoid and treat life-threatening hypoxemia. In the PICU, oxygen supplementation is a critical part of treatment for critically ill children with bronchiolitis. High-dose oxygen can have negative consequences.[2] Researchers aimed to characterise the pulmonary (local) and arterial (systemic) oxygen exposure during invasive mechanical ventilation (IMV) in children with severe bronchiolitis in this study.

In patients with severe bronchiolitis who required invasive mechanical ventilation, moderate to high-dose pulmonary oxygen exposure and potential oxygen overuse were common.

Methods:

This was a Single-centric Retrospective cohort study. Children under the age of 2 who had severe bronchiolitis and a received IMV are admitted to the PICU ere included in the study. Researchers gathered information on the patient's characteristics, outcomes, hourly nurse-validated ventilator data up to the tenth cumulative day of IMV, and arterial blood gas analysis findings. Up to day 10 of IMV, arterial blood gas data, Fio2 and peripheral oxygen saturation (Spo2) hourly readings, and were all collected.

Variable (Time-Weighted Averages per 24-hr Window)	*n* Days[a]	*n* Subjects[b], 1 d	*n* Subjects[b], 2–3 d	*n* Subjects[b], > 3 d	Total Subjects[b], ≥ 1 d
Spo_2, *n* (%)					
< 92%	9 (0.9)	3 (1.7)	2 (1.1)	0	5 (2.8)
Fio_2, *n* (%)					
0.3–0.49	695 (70.4)	12 (6.8)	65 (36.9)	95 (54.0)	172 (97.7)
≥ 0.50	246 (24.9)	32 (18.2)	32 (18.2)	25 (14.2)	89 (50.6)
Pao_2[c], *n* (%)					
> 100 Torr (13.3 kPa)	38 (7.0)[d]	22 (15.7)[e]	7 (5.0)[e]	0	29 (20.7)[e]
> 248 Torr (33 kPa)	0	NA	NA	NA	0
CEE (Spo_2 ≥ 97%)[f], *n* (%)					
0.17–0.25	131 (13.3)	63 (35.8)	26 (14.8)	3 (1.7)	92 (52.3)
> 0.25	46 (4.7)	15 (8.5)	8 (4.5)	3 (1.7)	26 (14.8)
CEE (Spo_2 ≥ 95%)[g], *n* (%)					
0.17–0.25	283 (28.7)	52 (29.5)	68 (38.6)	16 (9.1)	136 (77.3)
> 0.25	174 (17.6)	41 (23.3)	27 (15.3)	15 (8.5)	83 (47.2)

Summary of Time-Weighted Averages per 24-Hour Window of Ventilator-Related Data

Results:

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In total, 24,451 hours of IMV were recorded in 176 individuals (median age, interquartile range (IQR), 1.0-2.3 mo). The first day of IMV had the largest pulmonary exposure to oxygen (median time-weighted average [TWA]-Fio2 0.46 [IQR, 0.39-0.53]), which markedly reduced during the following days. As severe hyperoxemia (TWA-Pao2 > 248 Torr [> 33 kPa]) was not detected, the systemic exposure to oxygen was rather low. But 52.3% of patients (n = 92) had at least one day of potentially excessive oxygen exposure, and 14.8% (n = 26) had a severe exposure. In addition, larger oxygen doses were associated with increased oxygen usage ($r_{\text{repeated measures}}$, 0.59; 95% CI, 0.54–0.63). Additionally, when Spo2 was greater than or equal to 97%, caregivers were more likely to maintain Fio2 above or equal to 0.50.

Discussion:

Researchers discovered that the majority of the 176 children in this retrospective cohort who underwent IMV for severe bronchiolitis had moderate to high levels of local oxygen exposure while having relatively low levels of systemic oxygen exposure. Furthermore, it was thought that oxygen exposure was frequently potentially excessive and almost certainly avoidable. [2]Researchers discovered that a potential rise in oxygen overuse was connected with an increase in oxygen dosage. The pilot trial for Oxygen in Pediatric Intensive Care (Oxy-PICU) liberal 's oxygenation arm was similar to the pulmonary oxygen exposure that was seen in this study.[3]

Conclusion:

In children with severe bronchiolitis on IMV, moderate to high doses of pulmonary oxygen exposure and potential oxygen overuse are frequent. Future research is required to determine the optimal oxygenation targets to limit oxygen exposure, as both of these have previously been linked to poorer outcomes in critically ill infants.

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4. A case report of a 2-month-old infant with RIT1-associated Noonan syndrome and dilated coronary arteries

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Introduction:

Noonan syndrome is a genetically inherited condition with a wide range of phenotypic symptoms. Gene mutations affect the RAAS/MAPK (mitogen-activated protein kinase) signalling pathway.[1,2] Patient manifestations can be mild or severe. The phenotypic features of Noonan syndrome can vary and can alter with age. It is typically a genetically inherited condition. Wide-set eyes, low-set ears, short stature, and pulmonic stenosis are the symptoms that are most common. Normal autosomal dominant inheritance is the mode of inheritance for Noonan syndrome. [2] Noonan Syndrome phenotypic variability has increased with the discovery of more causative genes, including congenital cardiac abnormalities. Here is a report of study on this uncommon Noonan Syndrome presentation by describing a case of dilated coronary arteries in a young patient with a RIT1 variation.

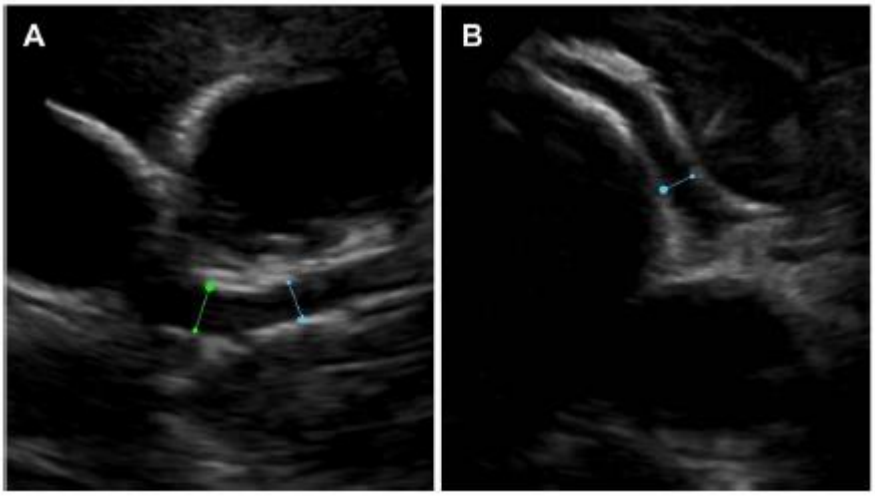
This case highlights the significance of the association between dilated coronary arteries and Noonan

.

Case Presentation:

This patient, a 2-month-old female, was born spontaneously at 36 weeks' gestation after a challenging pregnancy involving polyhydramnios of unclear cause that required multiple amnioreductions. Amniotic fluid was subjected to genetic testing, and neither karyotype nor FISH analysis revealed any anomalies. The mother's test results for polyhydramnios-related infections were negative. There was a small muscular ventricular septal defect(VSD) visible on a prenatal echocardiogram. A day after birth, an echocardiography revealed a mildly dilated proximal left anterior descending artery (LAD) with a z-score of 3.3 and borderline dilation of the left main coronary artery (LMCA) with a z-score of 2.0. The delivery and postnatal course were unremarkable. A coronary artery abnormality is indicated by a z score for the internal lumen diameter ≥ 2.5 , according to American Heart Association (AHA) recommendations. At first, it was assumed that the coronary artery dilation was caused by brief episodes of foetal supraventricular tachycardia, which would normally go away after delivery. To keep an eye on the heart problems, the patient frequently visited cardiology for follow-up sessions. She was discovered to have valvular dysplasia at the age of 2 weeks and an elevated gradient across her pulmonary valve (52 mmHg). With z-scores of proximal LAD

7.2, LMCA 3.8, and right coronary artery (RCA) 3.7, an echocardiography performed at 2 months of age revealed a considerable increase in coronary dilation compared to her prior echocardiograms.



A Echocardiogram images at 2 months of age showing dilated coronary arteries—left main coronary artery and proximal left anteriordescending and **B** right anterior descending

Despite her appearing to be in good clinical condition, inflammatory markers were drawn to rule out MIS-C or Kawasaki disease. The results showed significant levels of pro-BNP (622 ng/L, 5-450 ng/L), ferritin (409 ng/mL, 50-200 ng/mL), WBC (14.23 106/L, 6-180 103/uL), platelets (936 103/µL), erythrocyte sedimentation rate (ESR She was admitted directly from the outpatient cardiology clinic for additional assessment due to the raised pro-BNP, elevated ferritin, and elevated platelets along with the elevated z-scores. The patient's vital signs were normal at the time of admission. The physical examination revealed some coarse facial features, low set ears, upslanting palpebral fissures, a flattened midface, a sloping forehead, and anteverted nares in a female infant who was not in immediate distress. IgA, IgM, IgE, C3, C4, a cytokine panel, and ANA were among the additional tests performed; all of the results were normal. The patient was treated for Kawasaki disease as a probable reason for her abrupt increase in coronary artery dilatation, even though her mother denied having recently had fever, rash, conjunctival redness, or any other indications of sickness.She received one dose of IVIG (2 g/kg) and began taking 81 mg of aspirin every day. She had a 39.5 °C fever about 13 hours after her IVIG treatment was completed. A urine sample was taken, and the results revealed 10 WBC/hpf, a small number of bacteria, nitrites, and blood. Blood and urine cultures were obtained. CRP was increased again, this time at 13.8 mg/L. Her ceftriaxone treatment was stopped after 48 hours since her cultures showed no growth. Given the results of her echocardiography and her dysmorphic facial features, genetics was also consulted, and on the second day of her stay, rapid whole genome sequencing (rWGS) was sent. The most at-risk populations are benefiting from the use of rWGS, a new technology that frequently diagnoses genetic disorders early enough to have an influence on medical therapy. Her non-specific and complicated phenotype, as well as the uncertainty of her hospital course, necessitated the start of this testing. On the fifth day after admission, the patient underwent a coronary angiography to better evaluate her coronary arteries and conduct a balloon valvuloplasty on her pulmonary valve. Additionally, on day 5 after admission, preliminary rWGS data showed that RIT1,

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a rare cause of Noonan syndrome, had a potential pathogenic variation. Only 69 hours after blood was obtained to start the rWGS testing, this diagnosis was made. Clinical phenotype of the patient supported this diagnosis. During her inpatient stay, the patient's inflammatory markers remained elevated, and rWGS data was reanalyzed to make sure the patient didn't have a second genetic mutation that was the cause of a different ailment or syndrome. This was accomplished utilising data analysis filters that examined inflammatory and autoimmune genes. There was no secondary diagnosis, which was confirmed by the lack of new genome-related discoveries. The patient was discharged home the following day due to the RIT1 variant diagnosis, which also provided assurance regarding her cardiac results.

Discussion:

RIT1 is one of several genes that have been linked to Noonan syndrome, but variations in RIT1 are less frequent in Noonan syndrome than in other known genes.[3] Adding another case to the body of literature is crucial for the medical management of these patients because cardiac deformities in patients with Noonan syndrome caused by RIT1 gene mutation are frequently reported, but there are few cases of coronary artery abnormalities in children with Noonan syndrome.[1]

Conclusion:

This case emphasises the importance of the link between Noonan syndrome and dilated coronary arteries and suggests that people with Noonan syndrome should undergo thorough cardiac screening. This instance also demonstrates the significance of interacting with experts in various subspecialties before determining a diagnosis. With the help of multidisciplinary medicine, the patient was able to receive a diagnosis and the assurance, despite having dilated coronary arteries and high inflammatory markers, her health was not at immediate risk.

Reference:

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