

Partial Trisomy 16q21-q24.3 with Novel Cardiac Manifestation of Left Ventricular Noncompaction Cardiomyopathy: A Case Report

Aradhana Dwivedi¹ Vivek Kumar² H. Ravi Ramamurthy²

¹Department of Medical Genetics, Army Hospital (Research and Referral), New Delhi, India

²Department of Pediatric Cardiology, Army Hospital (Research and Referral), New Delhi, India

Address for correspondence Vivek Kumar, MD, DNB, FPC, Department of Pediatric Cardiology, Army Hospital (Research and Referral), Dhola Kuan, Delhi Cantonment, New Delhi 110010, India (e-mail: vk3532@gmail.com).

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Abstract

Keywords

- partial trisomy 16
- left ventricular noncompaction
- cardiomyopathy

Partial trisomy 16q is most often a consequence of malsegregation from a balanced parental translocation involving chromosome 16q. It is characterized by nonspecific craniofacial dysmorphic features, hypotonia, developmental delay, psychomotor retardation, and systemic manifestations of cardiac defect, renal abnormalities, and lung abnormalities. The survival of these patients depends upon the extent and severity of the organs involved. The present literature was replete with cases of partial trisomy 16q having structural cardiac defects. However, in the present report we described a novel finding of myocardial disease in the form of left ventricular noncompaction (LVNC) cardiomyopathy associated with this genetic condition.

Introduction

Trisomy 16 spectrum extends from full trisomy¹ to mosaic² to partial trisomy of long and short arms.³ Full trisomy 16 always leads to first trimester spontaneous abortion; however, postnatal survival of partial trisomy 16 depends upon the severity of congenital defects. Unbalanced segregation of balanced parental translocation results in partial trisomy 16. The clinical features of partial trisomy of the long arm of chromosome 16 include low birth weight, hypotonia, failure to thrive, psychomotor retardation, microcephaly, and non-specific craniofacial dysmorphism in the form of periorbital edema, prominent forehead, low set ears, flat nasal bridge, antimongoloid slant, micrognathia, hypertelorism, long philtrum, and cleft palate. Systemic abnormalities consist of congenital heart defects, renal abnormalities, lung abnormalities, and gall bladder agenesis.⁴ Previously structural cardiac defects have been reported in partial trisomy 16. We herein described an unusual and novel finding of left ventricular noncompaction (LVNC) cardiomyopathy in a case with partial trisomy 16.

Case Report

A 22-month-old female toddler, firstborn of nonconsanguineous marriage, brought by her parents with concerns of delayed milestones and failure to thrive since early infancy. Antenatal history was unremarkable. She was born at term, with a birth weight of 1.7 kg (small for gestational age). Neonatal period was uneventful and family history was not contributory.

On examination, vital parameters including pulse, blood pressure, and SpO₂ were normal. Her height and weight were below 3rd percentile. Head circumference was below –3SD (microcephaly). She was noted to have dysmorphism in the form of high prominent forehead, periorbital edema, cleft palate (surgically corrected at 9 months of age), bitemporal narrowing, epicanthal folds, antimongoloid slant, and clinodactyly. Her development was estimated at around 14 months of age. Neurological examination revealed hypotonia with normal reflexes. Cardiovascular, respiratory, and abdominal system examinations were unremarkable. Hearing and eye evaluation did not reveal any abnormality. Hematological and biochemical parameters including thyroid function were

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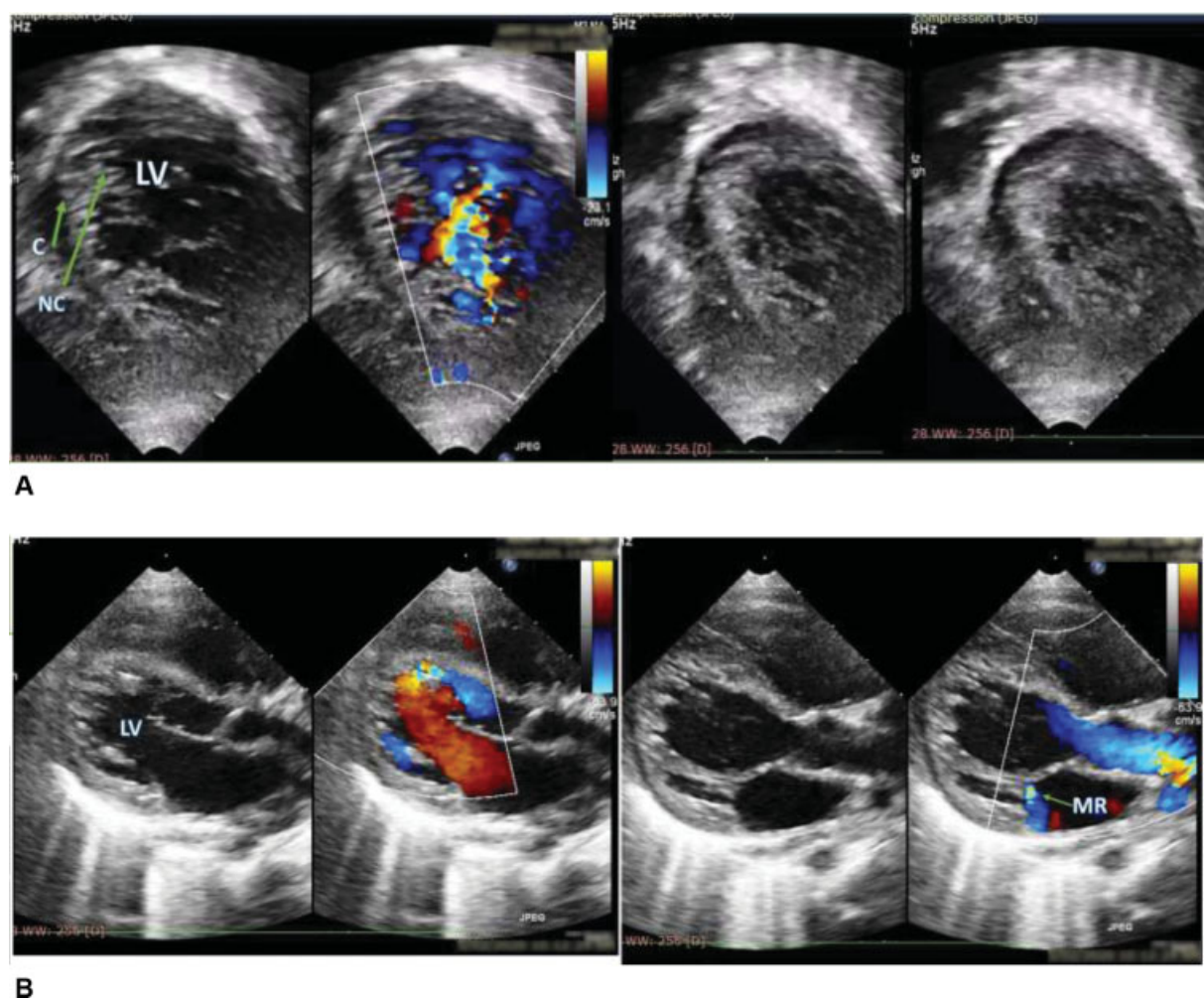


Fig. 1 Parasternal short axis view; two-dimensional (2D), color Doppler image in diastole on the left shows compacted (C) and noncompacted (NC) region on the septum and free wall of the left ventricle (LV) with color flow in intertrabecular recesses; two systolic frames on the right are delineating the extent of noncompacted LV. Parasternal short axis view; 2D, color Doppler image in diastole on the left and systole on the right shows apical and free wall NC of LV with mild mitral regurgitation (MR).

within normal limits. Skeletal survey and ultrasonography of the abdomen and pelvis did not show any anatomical or structural abnormality.

Echocardiography showed structurally normal heart with LVNC on the septum and on posterior and free walls in parasternal short axis. Noncompaction to compaction ratio was >2 . Parasternal long-axis view showed LVNC in the apical region and posterior wall with mild mitral regurgitation. M-mode showed left ventricular (LV) ejection fraction of 63% (normal) and left ventricular internal dimension in diastole 28 mm (z score 1.3; LV size was normal; ▶Fig. 1A, 1B; ▶Video 1). Echocardiography of the parents did not reveal any abnormality.

Video 1

Parasternal short-axis view showing left ventricular noncompaction involving the septum and the free wall. Online content including video sequences viewable at: <https://www.thieme-connect.com/products/ejournals/html/10.1055/s-0040-1714362>.

In view of failure to thrive, developmental delay, and dysmorphism (not conforming to a single gene disorder), the presence of unbalanced chromosomal anomaly should be considered, and thus a chromosomal microarray (CMA) was ordered. CMA analysis showed a duplication of 30, 304 kb (~ 30 Mb) on 16q21-qter (▶Fig. 2), consistent with a partial trisomy 16. Maternal karyotype revealed a balanced translocation between chromosomes 4q and 16q, 46,XX,t(4;16)(q34;q21), with breakpoints at 4q34 and 16q21(▶Fig. 3). Paternal karyotype was normal.

Discussion

Our patient with trisomy of 16q21-q24.3 had a craniofacial dysmorphism consistent with the phenotypic features of partial trisomy 16. Analysis of the published data has shown that most of the patients with partial trisomy 16 have heart defects and patients with larger trisomic segments have more incidence of congenital heart defects.⁵ Common congenital heart diseases reported with partial trisomy 16 include ventricular septal defect, atrial septal defect (ASD), patent ductus arteriosus (PDA), coarctation of



Fig. 2 Chromosomal microarray karyogram showing duplication corresponding to partial trisomy 16.

aorta, and interatrial septum aneurysm^{6–12} (►Table 1). However, Mishra et al¹³ for the first time had reported a case of partial trisomy 16q21-qter with complex cardiac abnormalities that included double outlet right ventricle, PDA, ASD, pulmonary stenosis, and bilateral superior vena cava. To the best of our knowledge, this report is the first case of partial trisomy 16 with LVNC cardiomyopathy. LVNC is a genetically heterogeneous condition, caused by patho-

genic variation in more than one gene (e.g., MYH7, MYBPC3). It was also reported in association with other Mendelian disorders (Noonan syndrome, Sotos syndrome, etc.) and various chromosomal disorders such as 1p36 deletion, 22q11.2 deletion, or trisomy 13. The association of a partial trisomy 16 and LVNC has not been established. LVNC is a disorder of endomyocardial morphogenesis due to the arrest of the normal compaction process of developing myocardium and is characterized by prominent trabeculations with deep intertrabecular recesses.^{14,15} Though there are multiple echocardiographic indices, it is commonly diagnosed by

The following paragraph needs revision. I have no clue what the authors are trying to say. It is kind of a mess.

Jenni et al described a diagnostic criterion that states that in the absence of coexisting cardiac structural abnormality, ratio of thick noncompacted layer to thin compacted layer is ≥ 2 and perfused intertrabecular recesses are supplied by intraventricular blood on color doppler analysis.¹⁶ Isolated LVNC with normal systolic function has the best outcome.¹⁷ However, LVNC with congenital heart disease is associated with more extensive trabeculations, worse systolic function, and genetic abnormalities.¹⁸ Our patient needs to be monitored for LV systolic dysfunction, thromboembolic episodes, and arrhythmias, which pose a significant risk to the health.¹⁹

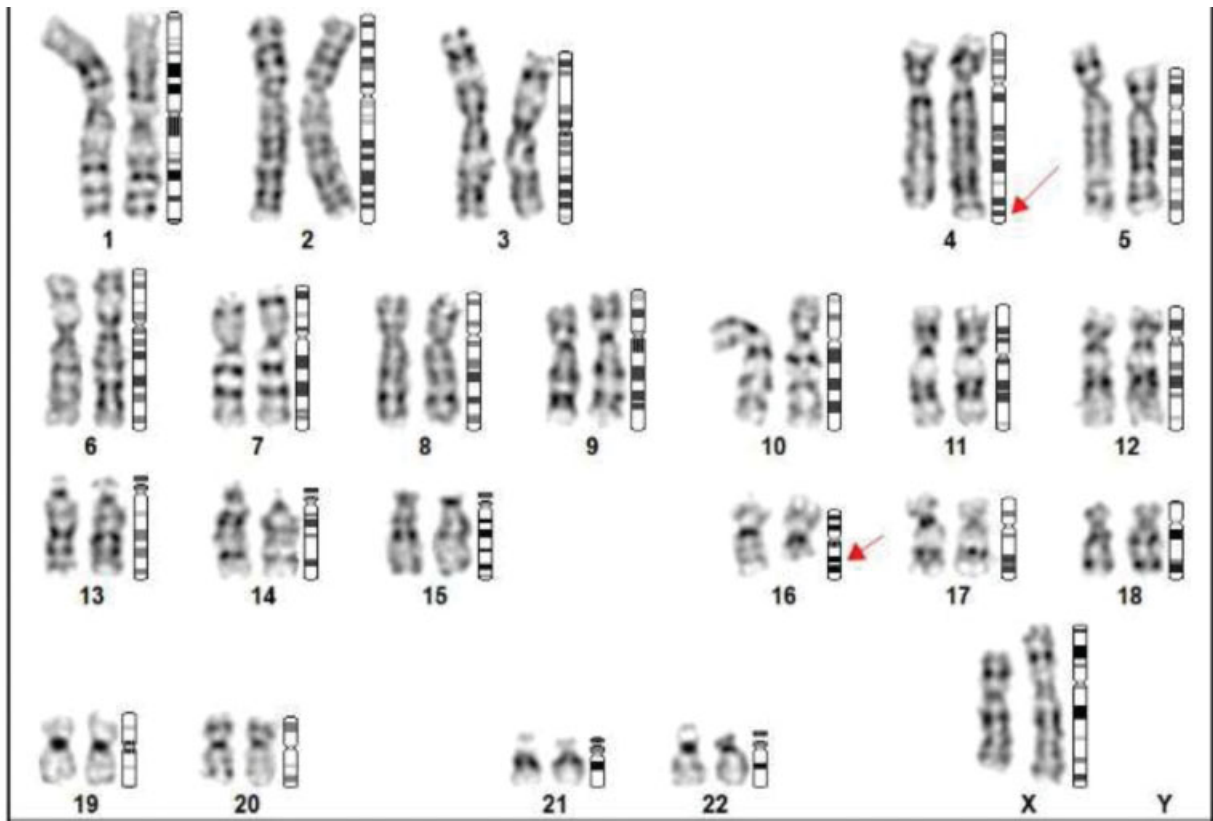


Fig. 3 Karyotype of proband's mother showing balanced translocation between the chromosomes 4 and 16, involving the regions q34 and q12.2, respectively.

Table 1 Genetic and cardiac defects of present case and comparison with previously reported cases

	Present case	Mishra et al ¹³	De Carvalho et al ¹²	Paladini et al ¹⁰	Hatanaka et al ⁹	Davison and Beesley ¹¹	Nevin et al ⁸	Ridler and McKeown ⁷	Francke ⁶
Trisomy	16q21-q24.3	16q21→qter	16q21→qter	16q12.1→qter	16q13→qter	16q13→qter	16q11→qte	16q21→qter	16q?
Parental translocation	t(4;16)(q34;q12.2) mat	(15;16)(p13;q21) mat	t(4;16)(q32;q21) mat	T(16;20)(q12.1;p13) pat	t(11;16)(q25;q13) pat	t(16;20)(q13;p13) pat	t(15;16)(p12;q11) mat	t(15;16)(p11;q11) mat	t(16q;22q) pat
Sex	Female	Female	Female	Male	Female	Female	Male	Female	Female
Cardiac defects	LVNC	DORV, VSD, PS, PDA, B/L SVC	Aneurysm of interatrial septum	ASD, VSD, CoA	ASD, PDA	VSD	PDA	ASD	PDA
Survival	22 mo (Alive)	10 mo	7 y (Alive)	10 d	6 mo	5 wk	5 wk	12 d	12 mo

Abbreviations: ASD, atrial septal defect; B/L SVC, bilateral superior vena cava; CoA, coarctation of aorta; DORV, double outlet right ventricle; LVNC, left ventricle noncompaction; mat, maternal; pat, paternal; PDA, patent ductus arteriosus; PS, pulmonary stenosis; VSD, ventricular septal defect.

Conclusion

Partial trisomy 16q should be suspected in the presence of characteristics craniofacial dysmorphism, failure to thrive, developmental delay and systemic anomalies. This genetic disorder is associated with multiple structural cardiac defects. We herein reported a novel cardiac finding of LVNC cardiomyopathy in partial trisomy 16q. This isolated report does not support a causal association as LVNC has multiple etiologies. We need more reports to substantiate this connection. However, it is pertinent to monitor patients with partial trisomy 16q for the myocardial diseases besides structural heart diseases.

Funding

None.

Conflict of Interest

None declared.

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