Marfan syndrome in a Triplo-X girl: A new association?

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Syndrome de marfan chez une fille porteuse d'un syndrome Triplo X: Une nouvelle association

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RÉSUMÉ

Prérequis: Le syndrome Triplo X est définit par la présence de trois chromosomes sexuels réalisant un caryotype 47 XXX. La majorité des patientes porteuses de ce syndrome ont un phénotype et développement mental normaux ou de discrètes anomalies dont certaines sont communes au syndrome de Marfan.
But: Rapporter une association inhabituelle de Triplo X syndrome et d'un syndrome de Marfan chez une fille.
Observation: Nous rapportons l'observation d'une fille porteuse d'un Triplo X qui présente des anomalies morphologiques et squelettiques qui se sont complétées durant le suivi réalisant une maladie de Marfan.
Conclusion: cette association n'a jamais été rapportée dans la littérature à notre connaissance. Certaines anomalies observés dans le syndrome triplo X sont également retrouvées dans la maladie de marfan. Ainsi chez ces patientes un suivi et une exploration sont nécessaires car le tableau de la maladie de marfan peut être incomplet au jeune âge.

Mots-clés

Anomalies - Génetique Syndrome de marfan

SUMMARY

Background: Triple X is a sex chromosomal abnormality that involves the presence of three sex chromosomes resulting in 47, XXX karyotype. Most patients suffering from this syndrome are usually mentally normal or subnormal with no gross malformation.
Aim: to report an unusual association between Triple X and Marfan disease in a girl.
Case report: A case of a triple X girl with craniofacial dysmorphy and skeletal anomalies, who did feat Marfan criteria by age, is presented.
Conclusion: To the best of our knowledge this association has never been reported. Some clinical features are common between Triplo X and Marfan disease so a careful follow-up is needed and investigations should be performed in these patients because Marfan syndrome may be incomplete in early age.

Key-words

Triple X - Marfan syndrome - Children

Triple X is a sex chromosomal abnormality that involves the presence of three sex chromosomes resulting in 47, XXX karyotype. The numerical abnormality occurs as a result of nondysjunction in meiosis I. 90% of these cases are of maternal origin and 10 % of paternal origin. Association has been reported with advanced maternal age and gestational diabetes. It is usually of sporadic origin. Most of these cases do not manifest as structural anomaly. We report here a case of a triple X syndrome associated with Marfan syndrome in a girl. To the best of our knowledge, this association has never been reported before.

CASE REPORT

A 16-month-old girl, first sibling of a consanguineous marriage, was admitted to our department to manage dyspnoea with wheezing. She was born at full-term by normal delivery. There was no history of neonatal distress. The early psychomotor milestones were as follows: she attained social smile by two months; she could control her head by five months, sit without support by 9 months, and stand with assistance and spoken a few words by one year. She presented three episodes of wheezing which were improved by bronchodilators. She had no family history of asthma or mental retardation. On examination: her weigh was 10,5 kg, her size was 87cm (+ 4 SD), her cranial perimeter was 47cm (-0.7 SD). She had dolichocephaly, malar hypoplasia, a high arched palate, pectus carinatum , arachnodactyly, clinodactyly, hallus valgus, flat feet, long limbs and joint laxity. She had dyspnoea and wheezing and she was unable to stand up alone. She received inhaled bronchodilators with intravenous corticoids with favourable outcome. The karyotype showed Triplo X: 47, XXX. Echocardiography was normal. Cerebral Computed Tomography Scan showed dolichocephaly and brain atrophy (Figure 1,2). Ophtalmological examination was normal; at that time, this girl had a marfanoid habitus and did not fit the criteria of Marfan syndrome.

Figure 1: Brain Computed tomography Scan showing dolichocephaly

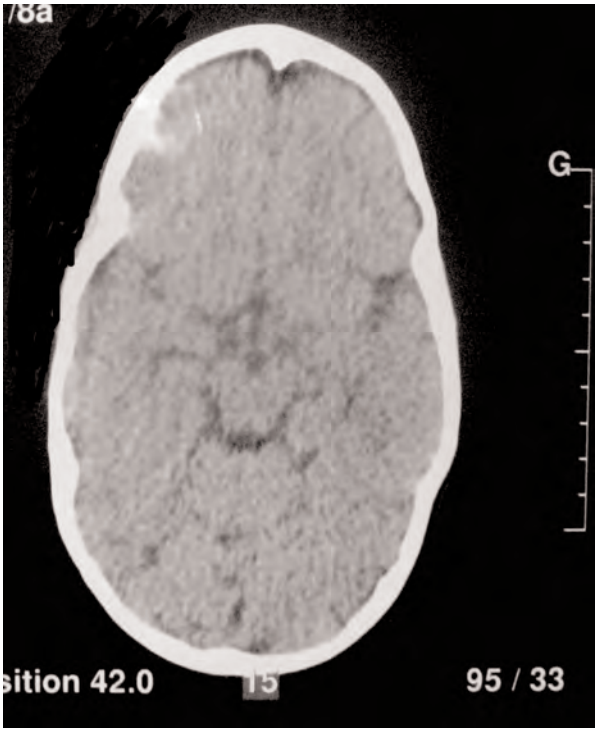
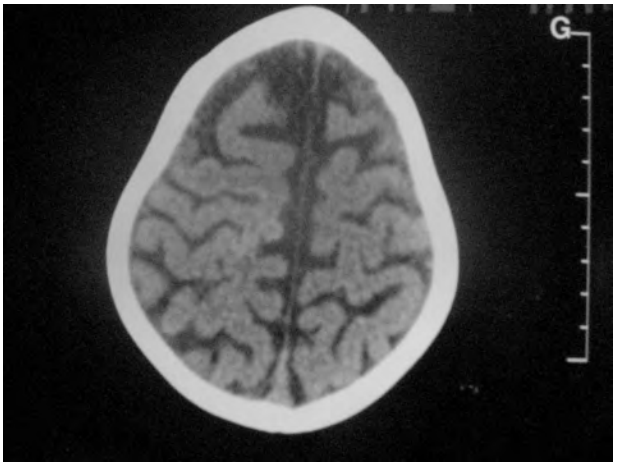


Figure 2: Brain Computed Tomography Scan showing brain atrophy



At the follow up, this patient developed cyphosis and scoliosis. She continued to present asthma attacks and received inhaled corticosteroid with incomplete improvement. Pulmonary function tests showed restrictive syndrome and bronchial hyperreactivity. Echocardiography showed at the age of nine years, ascending aortic dilatation, slight thickened atrioventricular valves and minimal mitral and aortic regurgitations without pulmonary hypertension. Ophtalmological examination was repeated and still normal. This patient walked at the age of two; she had learning disabilities, concentration and memory difficulties; she repeated the first and the second years of basic school. She had an intelligence quotient at the age of 6 of 100, which is rather normal compared to the median of age.

DISCUSSION

The triplo-X chromosome abnormality was first reported by Jacobs et al [1] in 1959. It occurs in approximately one out of 1000 newborn girls [2]. We have found reports in the review literature that vary so widely; however, most patients are usually mentally normal or subnormal with no gross malformation [3,4].

Craniofacial dysmorphy was reported in triple X syndrome; the patients presented, in various combination: epicanthus, depressed root of the nose, hypertelorism, small ears, high arched palate, cleft lip and palate, microcephaly or macrocephaly [5,6,7]. Our patient had high arched palate and dolichocephaly. Dolichocephaly has never been reported in

triple X syndrome but is reported in Marfan syndrome that constitute a minor criteria [8,9].

Various abnormalities of the skeletal system are mentioned in Triplo X syndrome patients. They include, in various combinations, kyphosis, scoliosis, abnormal size or shape of fingers, clinodactyly, pathology of the femoral head and club foot, tall stature [10,11,12]. Only a few cases with heart defects were reported in the literature in triple X syndrome: two patients had atrioseptal defect and one pulmonary artery stenosis [5]. Our patient had dolichocephaly, arachnodactyly, long limbs, hallus valgus, flat feet, joint laxity, scoliosis, cyphosis, tall stature, pectus carinatum and ascending aorta dilatation, mitral and aortic regurgitation that developed later at the age of nine. These clinical features fit the diagnosis of Marfan syndrome according to the criteria of the workshop of the International Congress of Human Genetics in Berlin 1986 [9]; yet, some of them are also reported in Triplo X syndrome ; to the best of our knowledge, this is the first case of Marfan syndrome in a triplo X girl.

Our patient had respiratory dysfunction. She had restrictive syndrome which is due to long bones overgrowth, scoliosis, and chest deformities (pectus carinatum) and authentic asthma attested by clinical manifestations and bronchial hyper-reactivity; There have been few previous studies of pulmonary function tests and only one of bronchial hyper-reactivity in Marfan Syndrome [13,14,15]. All patients tested in the series of König et al showed bronchial hyperreactivity and only one patient had asthma [13]. This pulmonary dysfunction is probably due to a dysregulation growth factor B activity as a result of mutations in fibrillin-1, a component of extracellular microfibrils, in Marfan's syndrome [16]. Further investigations may lead to new clues in the pathogenesis of both asthma and Marfan disease.

Others anomalies were reported in Triplo X syndrome: hydronephrosis due to ureteral stricture, bilateral polycystic kidney, jejunal atresia, duodenal atresia, auditory defect, bilateral optic atrophy and chorioidoretinitis [5]. None of these anomalies were seen in our patient.

Rovey et al examined 11 triples X girls ranging in age from 8 to 11 years to focus on to their performance in verbal non verbal and memory tasks; The results showed that the triple X girls were markedly inferior in their performance on these tasks, indicating a rehearsal deficit, an inability to use list structures, and weaker language skills compared to their normal siblings [17]. Tennes et al compared the development of 11 girls (ages 2-10 years) with 47,XXX karyotype identified in a newborn survey with eight girls having a mosaic sex chromatin pattern and with the normal siblings of each group; Delay in early motor development and speech, a mild intellectual deficit, and disturbance in inter-personal relationships occurred in one-third of the index cases, a higher frequency than in the comparison groups and two-thirds were considered normal and adequately adjusted [18].

Epileptic seizures were also mentioned in triplo X syndrome subjects [19]. Our patient had a delay in early motor development and speech. She had learning disabilities and concentration and memory difficulties; however her intelligence quotient was normal. Only a few cases with brain anomaly have been reported so far in Triplo X syndrome: agenesis of olfactory bulbs and tracts, hydrocephalus and schizencephaly; our patient had cortical atrophy [5, 20].

CONCLUSION

This is the first report of the association between Marfan syndrome and Triplo X syndrome. Some clinical features are seen in both Marfan syndrome and Triplo X syndrome such as tall stature, cyphosis, scoliosis, high arched palate, fingers anomalies, hallus valgus. Within this framework, a careful follow-up is needed and investigations should be performed in Triplo X patients who carry some of these features because Marfan syndrome may be incomplete in early age.

Références

1. Baran S, Igny A, Igny I. Respiratory dysfunction in patients with marfan syndrome. J Physiol Pharmacol 2007, 58, Suppl 5: 37-41
2. Barr ML, Sergovich FR, Carr DH, Shaver EL. The Triplo-X Female: An Appraisal Based on a Study of 12 Cases and a Review of the Literature. Canad Med Ass J. 1969 ; 101 :247-257
3. Beighton P, De Paepe A, Danks D, et al. International nosology of heritable disordres of connective tissue. Am J Med Genet. 1988;29:481-594
4. Ehara H, Eda I. Schizencephaly in triple-X syndrome. Pediatr Intern. 2001; 43, 296–7
5. Friedrich U, Nielsen J. Chromosome studies in 5,049 consecutive newborn children. Clin Genet. 1973;4:333-43
6. Gilgenkrantz S, Gilgenkrantz JM, Fauchier JP, Pierson M. A case of XXX syndrome with multiple malformations. Ann Genet. 1966 ; 9:123-6
7. Guichet A, Briault S, Moraine CL, Turleau C. Trisomy X: ACLF (Association des Cytogénéticiens de Langue Française) retrospective study. Ann Genet. 1996; 39: 117–22
8. Hamerton JL, Jagiello GM, Kirman BH. Sex-chromosome abnormalities in a population of mentally defective children. Br Med J. 1962 ;1:220-3
9. Jacobs PA, Baikie AG, Court Brown WM, et al. Evidence for the existence of the human "superfemale." Lancet. 1959; 2:423-5
10. Jagadeesh S, Jabeen G, Bhat L, et al.Triple X Syndrome with Rare Phenotypic Presentation. Indian J Pediatr. 2008; 756 : 629-31
11. Judge DP, Dietz HC. Marfan's syndrome. Lancet. 2005; 366: 1965–1976
12. Kanaka-Gantenbein C, Kitsiou S, Mavrou A, et al. Tall stature, insulin resistance, and disturbed behavior in a girl with the triple X syndrome harboring three SHOX genes: offspring of a father with mosaic Klinefelter syndrome but with two maternal X chromosomes. Horm Res. 2004;61:205-10
13. König P, Boxer R, Morrison J, Pletcher B. Bronchial hyperreactivity in children with Marfan syndrome . Pediatr Pulmonol. 1991;11:29-36
14. Liebezeit BU, Rohrer TR, Singer H, Doerr HG. Tall stature as presenting symptom in a girl with triple X syndrome. J Pediatr Endocrinol Metab. 2003;16:233-5
15. Morgan AW, Pearson SB, Davies S, Gooi HC, Bird HA. Asthma and airways collapse in two heritable disorders of connective tissue. Ann Rheum Dis 2007;66:1369-1373

16. Pfeiffer RA, Palm D, Jochmus J. The clinical aspects of trisomy of the X-chromosomes in adolescents (triple X-syndrome). Monatsschr Kinderheilkd. 1967 ;115:9-18
17. Rovet J, Netley C. The triple X chromosome syndrome in childhood: recent empirical findings. Child Dev. 1983;54:831-45.
18. Rovet J, Netley C, Bailey J, Keenan M, Stewart D. Intelligence and achievement in children with extra X aneuploidy: A longitudinal perspective. Am J Med Genet. 1995; 60: 356–63.
19. Tennes K, Puck M, Bryant K, Frankenburg W, Robinson A. Developmental Study of Girls with Trisomy X. Am J Hum Genet. 1975; 27:71-80
20. Wood JR, Bellamy D, Child AH, Citron KM. Pulmonary disease in patients with Marfan syndrome. Thorax. 1984;39;780-4