A Case of Triple-X Syndrome with Situs Inversus Totalis

Situs İnversus Totalisli Triple-X Sendromlu Bir Olgu

Abstract

Triple-X syndrome (47,XXX) is one of the most common aneuploidies. Most 47,XXX patients present with a normal phenotype except a tall stature. In 90% of the cases, additional X chromosome is of maternal origin. Additional X chromosome cannot explain phenotypic findings in triple X syndrome. Situs inversus totalis, resulting from an error during embryonic process, is characterized with complete mirror image transposition of abdominal and thoracic viscera. According to our best knowledge, an association of the triple-X syndrome and situs inversus totalis has not been described in the literature. In this article, we report a 9-month-old female with situs inversus totalis and 47,XXX karyotype.

Key Words: Situs inversus; triple X syndrome

Özet


Anahtar Kelimeler: Situs inversus; triple X sendromu


Triple X (47,XXX) syndrome is characterized by the presence of an additional X chromosome in the cells of a female. The incidence is 1/1000 to 1/1200 in female births. The ratio can increase with maternal age.1-3 Additional X chromosome occurs as a result of nondysjunction in maternal meiosis I.1 This chromosomal change typically does not cause abnormal physical features except tall stature. Delayed development of speech and language skills and learning disabilities are frequently seen in 47,XXX patients. Sexual orientation of these patients is normal.2,3

Situs inversus totalis is a rare congenital anomaly. It is characterized with complete mirror image transposition of abdominal and thoracic viscera.4 The incidence is 1/10 000 to 1/15 000.5 Hepatic, cardiac, esophageal, pancreatic, renal, pulmonary and vascular anomalies have been reported in patients with situs inversus totalis.4
Here, we report an infant with situs inversus totalis and 47,XXX karyotype. According to our best knowledge, an association of the triple-X syndrome and situs inversus totalis has not been described in the literature. Informed consent was obtained from the patient’s parents.

CASE REPORT

A 9-month-old girl followed with a situs inversus totalis since newborn period was referred to our hospital because of puffy face. Her delivery history was unremarkable. Her birth weight was 2700 g and height 47 cm. There was a close consanguinity between the parents. She was the first child of the family and had no sibs.

On physical examination, vital signs were normal. Her weight, height and head circumference were within the normal limits. She had sparse hair, brachycephalia, flat and large nasal bridge, thin lips, micrognathia, posterior rotated ears, and short neck. A Mongolian spot 5x5 cm in size was also noted on her hip. On thorax examination, a cardiac murmur was diagnosed. The reminder of physical examination was normal.

On laboratory examination, routine complete blood count, biochemical, renal and liver function test were within normal limits. Thyroid function tests were also normal. Echocardiography showed typical pattern of mirror image dextrocardia, large subaortic ventricular septal defect, patent foramen ovale, valvular pulmonary stenosis and anomalous systemic venous return. The diagnosis of situs inversus totalis was confirmed by abdominal ultrasonography. Chromosomal analysis performed on a peripheral blood lymphocyte culture showed a 47,XXX female karyotype.

DISCUSSION

In 47,XXX females, weight is lower, but length is higher than those of girls with normal chromosomes. In early ages, at 2-4 years of age, problems about skeletal maturation may be seen, but they become to normal limits at the age of 7-10.6 Although most patients have normal fertility and their children show normal karyotypes, a slightly increased risk for premature ovarian failure may be seen.2 Usually patients show no physical abnormalities but low intelligence quotient and difficulties in verbal skills can be seen.1,3,6 Sixty percent of the patients need special education in high school. Additionally, behavioral problems such as depression, communication disorders and less socialization are seen in 30% of the patients.3 An increased risk for cardiovascular disease has also been described.7

In this report, we presented a female with a 47,XXX karyotype and situs inversus totalis. Several cases have been reported with coincident situs inversus with many syndromes and congenital abnormalities such as Carpenter syndrome and polysplenia.8,9 Although many congenital malformations including urogenital tract, central nervous system, skeletal, craniofacial abnormalities and congenital heart defects have been reported in 47,XXX patients, situs inversus totalis, as in our case, has not been reported in the literature.

In the literature, X-linked laterality sequence has been well described.10,11 A submicroscopic deletion in Xq26 associated with familial situs ambiguous has been reported.12 Casey et al. reported that familial situs abnormalities were linked to a gene at Xq24-q27.13 Gebbia et al. showed that ZIC3 gene mutations were associated with X-linked situs abnormalities.14 In another study, ZIC3 mutations were found to be associated with congenital heart defects with or without heterotaxy.15 ZIC3 encodes a zinc-finger transcription factor. Several types of mutations (e.g frameshift, missense, nonsense) have been identified by Gebbia et al. and Ware et al. involving ZIC3 gene.14,15 Phenotypic expression of these mutations varies from isolated heart defects to situs inversus totalis according to the mutation type. S43X and K405E mutations in ZIC3 gene can be given as an example of these mutations. Although S43X mutation presents with classic heterotaxy, K405E mutation presents with congenital heart defect consistent with heterotaxy without other visceral anomalies.14,15

Our case had 47,XXX syndrome associated with situs inversus totalis and a large ventricular septal defect. Our findings suggest that abnormalities of X chromosome may be associated with situs inversus totalis.


