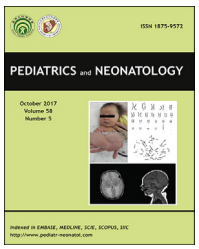
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Brief Communication

A newborn with monosomy X in association with corpus callosum agenesis

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1. Introduction

Turner syndrome (TS) is a genetic disease defined as a complete or partial absence of the X chromosome. The incidence of TS has been reported as approximately 1 in 2500 female births. TS is characterized by certain typical features, such as a short stature, primary amenorrhea, a webbed neck, cubitus valgus, lymphedema (particularly during infancy), and cardiovascular and renal abnormalities. Central nervous system (CNS) malformations are rarely seen in TS patients. Agenesis of the corpus callosum (ACC) has been described in only five patients with TS in the literature. We present the first patient with concomitant ACC and full TS diagnosed during the neonatal period.

2. Case report

We report a female infant born by cesarean section at 38 weeks of gestation. She was the second child of non-consanguineous parents. In the prenatal history, the maternal serum screening tests were normal. The mother had gestational diabetes and received medication during pregnancy. She received 10 U of neutral protamine Hagedorn at night and 3 U of regular insulin before every meal. Within the last months of pregnancy, fetal ultrasound examination was highly suspicious of ACC, and fetal magnetic resonance imaging revealed the presence of ACC. The birth weight was 3870 g (84.3 percentile), height was 52 cm (84.9 percentile), and head circumference was 36 cm (77 percentile). On a physical examination, retrognathia, downturned corners of the mouth, large ears, nuchal skin fold, inverted and widely spaced nipples, and lymphedema on the dorsum of her hands and feet were noted (Supplementary Figure 1). Results of a newborn hearing screening test were normal. Abdominal

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Table 1 Reported patients with Turner syndrome and corpus callosum agenesis

	Araki et al. (1987)[5]	Kimura et al. (1990)[6]	Abd et al. (1997)[4]	Lee et al. (2008)[3]	Pereira et al. (2014)[7]	Our case
Cytogenetic result	45,X	45,X	45,X/46,X, r(X) mosaic	45,X	46,X,+mar/45, X mosaic	45,X
Age (y)	14	19	8	32	Newborn	Newborn
Gonadal dysgenesis	UN	+	+	+	UN	+
Congenital lymphedema	UN	UN	−	−	−	+
Short webbed neck	+	UN	+	+	+	+
Short stature	+	+	+	+	−	−
Cubitus valgus	UN	UN	UN	+		+
Renal anomaly	+	+	−	−	−	−
Coarctation of aorta	−	−	−	+	−	−
Motor developmental delay	+	+	+	+	+	NR
Mental retardation/learning disability	Mild mental retardation	Severe mental retardation	Mild	Normal	NR	NR
Other anatomic CNS defects/neurological features						
Optic nerve hypoplasia	−	+	−	−	−	−
Hypotonia	−	+	−	−	+	−
Generalized joint laxity	−	−	+	−	−	−
Seizures	−	−	−	+	−	−

CNS = central nervous system; NR = not reported; UN = unknown.

ultrasound was unremarkable. Echocardiography revealed patent ductus arteriosus, patent foramen ovale, and mild aortic insufficiency. Brain magnetic resonance imaging showed ACC and wide lateral ventricles (Supplementary Figure 2). She had normal electroencephalography activity. Cytogenetic analysis revealed that the patient had a 45,X karyotype (Supplementary Figure 3). Written informed consent was obtained from the parents of the patient for the publication of this case report and accompanying images.

3. Discussion

The corpus callosum, which is a fiber tract connecting the two hemispheres in the brain, is the largest white matter structure in the CNS. Corpus callosum formation begins at six weeks of gestation, and its basic shape is completed at the age of 18–20 weeks. ACC is a common brain malformation with a prevalence of 0.5 per 10,000 in the general population.

It is reported that ACC has a heterogeneous etiology with both genetic causes and environmental factors, such as fetal alcohol syndrome or maternal phenylketonuria. The genetic causes of ACC include monogenic disorders and complex chromosomal rearrangements. Some of the patients with ACC have been diagnosed as having a genetic syndrome. Chromosomal abnormalities such as deletions, duplications, and aneuploidy have been described in ACC. Even though autosomal aneuploidy is more frequent, abnormalities of the X chromosome have been identified.[1,2]

CNS malformations, such as aberrant parietal cortex development, cerebellar vermis and pons hypoplasia, large fourth ventricle and cisterna magna, decreased parietal gray and occipital white matter, and increased cerebellar gray matter, are seen in TS patients.[3] These abnormalities may be related to visual–spatial functions and functional motor problems.

This is the first newborn patient reported with nonmosaic monosomy X and ACC. In this patient, characteristic features for a newborn with TS, such as a nuchal skin fold and lymphedema of the hands and feet, were present. Conversely, she did not have low birth weight and height, which may be associated with gestational diabetes or the coexistence of two different genetic conditions; this may have led to partial expression of both conditions. Additional characteristic features of ACC include seizures and hypotonia; feeding difficulties were not seen in this patient.[2] Mental problems and speech delay could not be assessed due to the age of the patient. Cytogenetic results and clinical features of patients reported as having TS concurrent with ACC are shown in Table 1.[3–7] ACC is a common brain malformation; there is no significant or specific finding between TS and ACC, which may be a coincidental association.

It has been reported that ACC is a part of several syndromes that have X-linked modes of inheritance. It has also been associated with chromosomal deletions of the X chromosome.[1,2] In humans, ~15% of X-linked genes escape X inactivation, and some of these genes may cause variable phenotypes of TS. Monosomy X associated with ACC is thought to be associated with haploinsufficiency of X-linked genes that escape inactivation.

In conclusion, we report on the first newborn to have nonmosaic (pure, 45,X) TS associated with ACC. More studies are required to understand genetic-background TS associated with ACC.

Conflicts of interest

None declared.

Appendix A. Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.pedneo.2016.05.006.

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