Chromosomal Foetal and Placenta Abnormalities Associated with Exomphalos and Umbicinal Hernia

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Abstract

Exomphalos is a rare congenital disorder demonstrated by failure of convergence mesoderm segments. Exomphalos is associated with congenital malformations and chromosomal abnormalities of autosomal or sex chromosomes and abnormalities with increased incidence in various systems such as renal and cardiovascular. The morbidity and mortality can be minimized by recognition of specific abnormalities associated with exomphalos development, the corresponding management and treatment strategies.

Conclusion: Exomphalos and umbilical hernias' may be associated with chromosomal abnormalities in autosomal and sex chromosomes and are related with genetic syndromes such as paternal uniparental disomy (UPD), Pallister-Killian (PKS) and Beckwith-Wiedemann syndrome.

Keywords: Exomphalos; Umbilical hernia; Chromosomal abnormalities; genetic syndromes; Abnormal karyotype

Introduction

Exomphalos separated in major and minor and could be associated with limb abnormalities, renal defects or caudal midline syndromes. Even though cardiac and renal defects are associated with the occurrence of exomphalos the prevalence is not yet associated with specific chromosomal abnormalities. Exomphalos may be associated with chromosomal abnormalities of both autosomal and sex chromosomes and other syndromes such paternal uni parental disomy (UPD), Pallister Killian (PKS) syndrome Beckwith-Wiedemann syndrome and feto placental chromosomal abnormalities (CMP). At this mini review study we will analyze the combination of exomphalos and umbical hernia with specific chromosomal abnormalities and genetic loci associated with the syndromes development.

Umbilical Hernia and Chromosomal Abnormalities of Autosomal Chromosomes

Umbilical hernia and exomphalos are rare congenital conditions with an incidence of 2-3 cases per 10,000 newborns and are associated with chromosomal abnormalities in foetus and placenta [1,2]. The risk of umbilical hernia and exomphalos varies according to maternal age, gestational age, type of birth and genetic disorders [3,4].

Trisomes 13 and 18 are the most common chromosomal abnormalities associated with the occurrence of umbilical hernia. Snijders et al. [3] determined the appearance of omphalocele in 22.5% of foetuses with trisomy 18, 9.1% of foetuses with trisomy 13, 12.5% of foetuses with other triploid chromosomal abnormalities while 0, 45% of embryos had no chromosomal defects. According to literature the risk factors such as Trisomes 18 or 13 in foetuses with omphalocele is 340 times higher comparing with embryos with no exomphalos during 11th to 14th weeks of gestational age [5,6].

Chen et al. [7] in a study of 89 cases of trisomies 18 revealed 12 cases with omphalocele (13.48%) estimated male to female ratio of 2:1 [7]. Blazer et al studied 18 foetuses with omphalocele and diagnosed 11 cases (61.1%) with chromosomal abnormalities, most cases related to trisomy 18, 21 and one case with fetal karyotype 45 X [6,7].

Calzolari et al. [1,2] analyzed 160 embryos and found 94 cases of umbilical hernia (58.8%) with concomitant chromosomal abnormalities. In 60 cases revealed trisomies 18, 23 or 13, four cases with trisomy 21 and seven with other chromosomal abnormalities [1,2].
Gilbert & Nicolaides [8] studied of 35 foetuses with omphalocele found that 19 had a chromosomal abnormality, 17 of them trisomy 18 and one karyotype type 47 XXY [8] while Brant berg in a study of 90 prenatally diagnosed omphalocele revealed 44 cases with chromosomal abnormalities most of them with trisomy 18, 13 and 21 [4,8]. Chromosomal abnormalities were found in majority of foetuses with central and epigastric omphalocele. On the other hand, Van de Geijn analyzed 22 foetuses with omphalocele and found 10 cases with autosomal chromosomal abnormalities, six with trisomies 18 and one with trisomy 13 [8,9].

Hughes et al. [10] studied 30 foetuses with omphalocele and found 13 cases who had chromosomal abnormalities. Most of the foetuses had trisomy 18, trisomy 13, two had a trisomy 21 and one Turner syndrome while Hwang & Kousseff [11] in a study of 93 cases of umbilical hernia found in 37 cases with chromosomal abnormalities, including trisomy 19, 18, 11, 21 and trisomy 13. Nicolaides et al. [6] in a study of 116 foetal of omphalocele revealed 42 cases (36.2%) of identified autosomal chromosomal abnormalities. Most of examined foetuses had trisomy 18, six had trisomy 13 [12].

Additionally, Eydoux et al. [13] in the one study of 46 embryos with omphalocele found that 12 cases (26.1%) had chromosomal abnormalities and seven trisomy 18, trisomy 13 while Hsu et al. [14] studied 24 neonates with omphalocele and reveal six cases (25%) with chromosomal abnormalities such as trisomy 18 and 13 [14].

Even if several studies revealed the correlation between umbilical hernia and trisomy 21; Torfs et al. [15] found only one case of trisomy 21 among 2979 newborns with omphalocele and concluded that trisomy 21 is not predispose of increased risk for umbilical hernia. Mastroiacovo et al. [16] revealed seven cases of trisomy 21 among 8560 cases of umbilical hernia. At this study the ratio was 1/1200 which was significantly higher than 1/425,000 of general population, suggesting that trisomy 21 increases the risk of umbilical hernia in fetus.

**Umbical Hernia and Sex Chromosomal Abnormalities**

Besides autosomal chromosomal abnormalities exomphalos and umbilical hernia can also be associated with chromosomal abnormalities of sex chromosomes such as monosomy 45 X and trisomies 47 XXY or 47 XXX [17-19]. In prenatal screening is important besides abnormalities of autosomal chromosomes to identify chromosomal abnormalities of sex chromosomes as possible key factors of umbilical hernia development.

Saller et al. [17] reported the presence of monosomy 45 X in a fetus with omphalocele while Govaerts et al. [18] identified a case of umbilical hernia in fetus with monosomy 45 X and polyhydramnion by ultrasound analysis during gestational age of 22 weeks. Goldstein & Drugan [19] suggested that umbilical hernia in patients with Turner syndrome may be due to expression of some localized genes of X chromosome in early pregnancy. Several reports suggested that chromosomal abnormalities are more common in combination with omphalocele [20,21] while the cysts of umbilical cord increase risk of aneuploidy occurrence, mainly of trisomy 18 in fetuses with omphalocele [21]. Cysts umbilical related omphalocele usually are pseudo cysts and allantoïd vesicles [21].

**Syndrome Pallister-Killian (PKS) and Umbilical Hernia**

Pallister-Killian (PKS) Syndrome is a malformation characterized by mosaicism and tetrasomy of 12p genetic region. The PKS has the clinical features of local alopecia, severe mental retardation, seizures and frequent occurrence of diaphragmatic hernia while in some cases it may be associated with omphalocele. Tejada et al. [22] have reported a case of PKS with ultrasonographic features such as polyhydramnion, umbilical hernia and short length diagnosed with tetrasomy of 12p confirmed in cell cultures of skin fibroblasts.

**Paternal Uniparental Disomy (UPD) of Chromosome 14 and Umbilical Hernia**

Paternal uniparental disomy (UPD) has been reported to be associated with multiple abnormalities such as thoracic hypoplasia, ribs abnormalities, laryngomalacia, hypertrophic cardiomyopathy and mental retardation [23]. Papenhausen et al. [24], Cotter et al. [25] and Kurosawa et al. [26] reported the correlation of umbilical hernia with occurrence of UPD of chromosome 14. Towner et al suggested that prenatal diagnosis of abdominal defect associated with increased nuchal translucency or skeletal abnormalities and coexistent of UPD of chromosome 14 [27].

Several abnormal characteristics are associated with UPD on different chromosomes. For example, genetic mapping on chromosome 11 and paternal UPD connected to Beckwith Wiedemann syndrome [28,29]. UPD of chromosome 15 has also been associated with the syndromes Prader Willi and Angelman [30] as well as the UPD of chromosome 16 may also associate with abnormal phenotypes [31,32].

**Micro duplication of Genetic Region 15q11**

According to literature referred a case report of a foetus with exomphalos, increased nuchal translucency and normal karyotype. The ultrasound analysis revealed exomalpos with micrognathia and tetralogy of Fallot. Although the karyotype was normal molecular karyotype revealed micro duplication of 408 kb in chromosomal region of 15q11.2.

**Beckwith-Wiedemann Syndrome (BWS) and Exomphalos**

BWS caused by impairments and deficiencies occurred in the chromosomal region of 11p15 [33-35]. This genetic region comprises the genes involved in the cell cycle, development and tumour suppression. The chromosomal location of 11p 15 is organized into two subareas comprising the genes IGF2 and H19 and another centromeric region includes genes CDKN1C (Kinase...
Inhibitor 1C), KCNQ1 (subfamily Q, potassium voltage-gated channels) and KCNQ1OT1 [34,35].

Mutations in CDKN1C gene (known as p57Kip2) demonstrated at 5% of patients with BWS [36]. Patients with mutations CDKN1C gene have a typical phenotype of BWS, with a very high frequency of exomphalos. The appearance of exomphalos associated quite strongly with the syndrome as 65% of patients with BWS may appear exomphalos [35,36].

Exomphalos occurrence is more frequent in patients with mutations in the genes KCNQ1OT1 and CDKN1C. If methylation status of KCNQ1OT1 and H19 genes is normal then sequencing analysis of CDKN1C is important especially in patients with family history of exomphalos [35,36].

Fetoplacental Chromosomal Abnormalities (CMP) and Exomphalos Development

The effects of chromosomal abnormalities in placental and foetus (CPM) are under investigation due to assess the participation of these genetic elements in exomphalos development [37]. CPM aberrations associated with growth retardation, and foetal death. The fetoplacental chromosomal abnormalities may lead to emergence of a different number of chromosomes of placenta and the foetus even if the karyotype is normal. These foetuses may reveal normal growth [38] or intrauterine growth restriction outcome that may result in intrauterine foetal death [39]. Drikos et al studied case of an infant diagnosed prenatally with exomphalos with intestinal contents from the 14th week of gestational age. Prenatal diagnosis by chorial villi sample detected pseudo-mosaicism of placenta (mos45X/46XY), while amniocentesis on the 19th week of pregnancy revealed normal karyotype. This is the first reported case of placental pseudo-mosaicism (mos45X/46XY) combined with exomphalos [38].

Trisomy 2 of the placenta associated with growth retardation and abnormal clinical characteristics at birth, while the CPM on the sex chromosomes does not usually have any adverse effect on embryo development [39]. The pseudo-mosaicism of placenta may also be associated with the occurrence of umbilical hernia and various phenotypic abnormalities. In a clinical case showed non mosaic trisomy 22 in the chorionic villus, mosaic trisomy 22 in amniocytes and normal karyotype of lymphocytes showed abnormal foetal characteristics of reminiscent Goldenhar syndrome. The foetal mosaicism appears to be the likely explanation for Goldenhar syndrome [39,40].

Conclusion

Exomphalos and umbilical hernia can quite often associate with disorders of the gastrointestinal and central nervous system seems to be predominated such as in cases of Beckwith-Wiedemann and abnormal karyotype syndromes.

Exomphalos may be associated with limb abnormalities or caudal midline syndromes. Although cardiac and renal abnormalities seem to be associated with the occurrence of exomphalos the prevalence is not apparently associated with chromosomal abnormalities. Such disorders may be associated with chromosomal defects at autosomal and sex chromosomes and other syndromes such as paternal uniparental disomy (UPD), Pallister-Killian (PKS) and Beckwith-Wiedemann syndromes. The determination of the associated malformations can lead to conscious prenatal counselling. This provides parents reliable and clear information’s in order to determine the continuation of pregnancy.

Compliance with Ethical Standards

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The author declares have no conflict of interest.

References


