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Lethal congenital arthrogryposis presents with increased nuchal translucency at 10–14 weeks of gestation

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ABSTRACT

This study examines the ultrasonographic features of congenital lethal arthrogryposis. In 27 cases of arthrogryposis diagnosed in the second and third trimesters there was severe bilateral talipes, fixed flexion deformities of the wrists and elbows and either fixed flexion or extension of the knees. In seven (26%) of the cases there was nuchal edema. In two fetuses with arthrogryposis that were examined at 13 weeks of gestation the nuchal translucency thickness was above the 99th centile of the normal range for crown–rump length. In three other women with previously affected pregnancies, ultrasound examination at 10–14 weeks demonstrated normal fetal nuchal translucency thickness and none of these fetuses were subsequently found to have arthrogryposis. These findings suggest that lethal arthrogryposis, which is usually diagnosed by the demonstration of multiple joint contractures during the second or third trimester of pregnancy, may present as increased nuchal translucency thickness at 10–14 weeks of gestation.

INTRODUCTION

Congenital lethal arthrogryposis is a heterogeneous group of conditions resulting in bilateral talipes and fixed flexion or extension deformities of the knee, elbows and wrists. Pathological studies have reported that these features are frequently associated with fetal myopathy, neuropathy or an underlying connective tissue abnormality[1–3]. Prenatal diagnosis is usually made by ultrasonography during the second or third trimester of pregnancy and is based on the demonstration of skeletal deformities. However, both sonographic and pathological studies have reported that in some fetuses with arthrogryposis there is nuchal edema[1,4], raising the possibility that the condition may present with increased nuchal translucency thickness at 10–14 weeks of gestation.

This study examined the sonographic features of arthrogryposis in 27 affected fetuses that were diagnosed during the second and third trimesters and also reports the findings of two fetuses that were examined at 13 weeks of gestation.

MATERIALS AND METHODS

The Harris Birthright Research Centre for Fetal Medicine is a referral center for fetal diagnosis and therapy. Data on demographic characteristics, obstetric history and ultrasound findings are entered into a computer database at the time of the ultrasound examination. Details on pregnancy outcome, which are obtained from the referring hospitals and the patients, are also entered into the database.

A computer search was made for patients with a previous pregnancy complicated by arthrogryposis who were referred to our center at 10–14 weeks for prenatal diagnosis. Transabdominal and transvaginal ultrasound scanning was carried out to measure the fetal crown–rump length and nuchal translucency thickness and to examine the fetal anatomy[5]. In those cases with no obvious defect at the initial scan, ultrasound examinations were repeated at 4-weekly intervals throughout the pregnancy, to look for any limitation of fetal movements and the development of joint abnormalities.

A computer search was also carried out for any cases of arthrogryposis presenting during the second or third trimester of pregnancy; in these cases a first-trimester scan had not been carried out.

RESULTS

During a 1-year period (November 1994 to November 1995), five patients with a previous pregnancy complicated by arthrogryposis were referred to our center at 10–14

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weeks of gestation (Table 1). In three cases there were no obvious fetal defects and the fetal nuchal translucency thickness was within the normal range for gestation[6]; in these cases there were no abnormal findings at the subsequent scans and healthy infants were delivered at term. In two cases the fetal nuchal translucency thickness was above the 99th centile for gestation (Figure 1) and detailed examination demonstrated bilateral fixed flexion deformities of the hands, wrists, elbows and knees as well as severe talipes. In both cases chorion villus sampling was carried out and the fetal karyotype was normal (46,XY). At the request of the parents, surgical termination of pregnancy was carried out. Postmortem examination confirmed the sonographic findings (Figure 2). Additionally, examination of the heart and great arteries demonstrated in both cases narrowing of the aortic isthmus with no intracardiac defect[7].

During an 8-year period (1987–1995), there were 27 pregnancies in which the diagnosis of arthrogryposis was made at 16–34 weeks in women who had not had a 10–14-week scan carried out (Table 2). The indications for referral in these cases were history of previous affected pregnancies ($n = 7$), polyhydramnios ($n = 8$) and fetal talipes ($n = 10$) or nuchal edema ($n = 2$). In all cases there were severe bilateral talipes, fixed flexion deformities of the wrists and elbows and either fixed flexion or extension of the knees (Figure 3). Additionally, seven (26%) had nuchal edema, five (19%) had pleural effusions, 11 (41%) had

Table 1 Ultrasound findings at 10–14 weeks of gestation and subsequent outcome of pregnancies with a previous history of arthrogryposis

Case	*Previous history*	*Gestation* (weeks)	*Nuchal translucency* (mm)	*Sonographic findings*	*Outcome*
1	TOP at 19 weeks	13	10.5	talipes and joint contractures	TOP at 14 weeks
2	2 NNDs at term	13	6.3	talipes and joint contractures	TOP at 14 weeks
3	TOP at 21 weeks	11	1.2	scans at 4-week intervals showed no abnormalities	LB at 38 weeks
4	TOP at 18 weeks 6 IUDs at 22–32 weeks*	12	1.8	scans at 4-week intervals showed no abnormalities	LB at 40 weeks
5	1 IUD at 35 weeks	12	1.2	scans at 4-week intervals showed no abnormalities	LB at 40 weeks

TOP, termination of pregnancy; IUD, intrauterine death; NND, neonatal death; LB, live birth of healthy infant; * same as case 7 of Table 2

Figure 1 Increased nuchal translucency thickness in a 13-week fetus with arthrogryposis

Figure 2 Photomicrograph of the hands of a 14-week fetus with arthrogryposis presenting at 13 weeks with increased nuchal translucency thickness

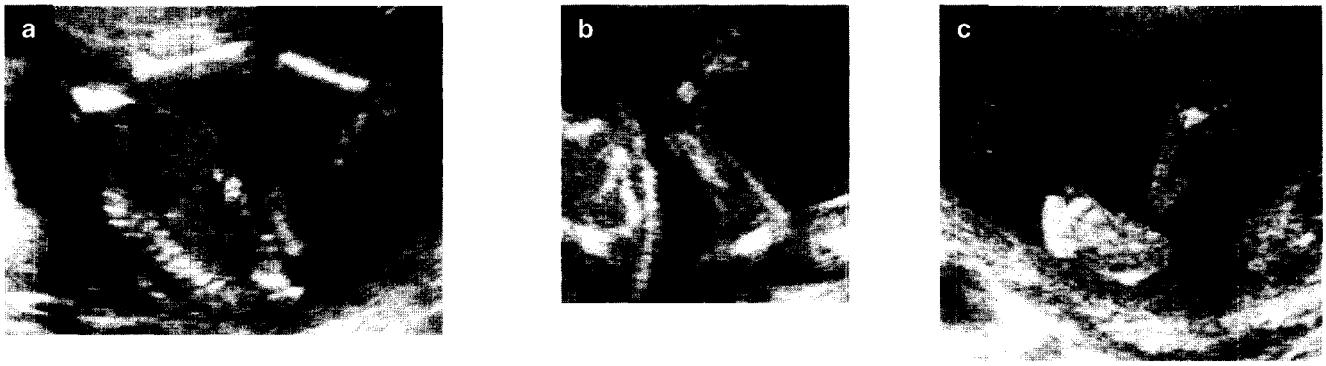

Figure 3 Extended knees (a), fixed flexion of wrists (b) and talipes (c) in a 19-week fetus with arthrogryposis

Table 1 Ultrasonographic features and outcome of pregnancies with lethal arthrogryposis diagnosed during the second or third trimester of pregnancy

		Ultrasonographic features					
Case	*Indication for referral*	*Gestation* (weeks)	*Ankles*	*Knees*	*Elbows and wrists*	*Other*	*Outcome*
6	history: TOP 21 weeks	17	talipes	extended	flexed		TOP at 16 weeks
7	history: 5 IUDs at 22–32 weeks, TOP 18 weeks	17	talipes	flexed	flexed	nuchal edema, pleural effusions, micrognathia and collapsed stomach	TOP at 17 weeks
8	history: IUD 24 weeks, NND 36 + 38 weeks	20	talipes	flexed	flexed	nuchal edema, micrognathia, hydronephrosis	TOP at 20 weeks
9*	history: TOP 27 weeks, IUD 30 + 32 weeks NND 32 + 34 weeks	17	talipes	extended	flexed		IUD at 30 weeks
10	history: NND 32 weeks	19, normal 22, abnormal	talipes	flexed	flexed		TOP at 22 weeks
11	history: IUD 39 weeks	19, normal, 23, abnormal	talipes	flexed	flexed	nuchal edema, micrognathia, ventriculomegaly, hydronephrosis	TOP at 23 weeks
12*	history: IUD 30 + 32 weeks, NND 32 + 34 weeks	19 + 23, normal, 27, abnormal	talipes	extended	flexed	collapsed stomach, polyhydramnios	TOP at 27 weeks
13	nuchal edema at 18 weeks	18	talipes	extended	flexed	nuchal edema	TOP at 18 weeks
14	nuchal edema at 19 weeks	19	talipes	extended	flexed	nuchal edema, micrognathia, ventriculomegaly	TOP at 19 weeks
15	talipes at 19 weeks	19	talipes	flexed	flexed	micrognathia, hydronephrosis	TOP at 20 weeks
16	talipes at 19 weeks	19	talipes	flexed	extended		TOP at 19 weeks
17	talipes at 20 weeks	20	talipes	extended	flexed	ventriculomegaly	TOP at 22 weeks
18	talipes at 20 weeks	20	talipes	flexed	flexed	nuchal edema and hydronephrosis	IUD at 30 weeks
19	talipes at 21 weeks	21	talipes	flexed	flexed	talipes at 21 weeks, joint contractures at 25 weeks, collapsed stomach and polyhydramnios at 29 weeks	NND at 32 weeks
20	talipes at 21 weeks	21	talipes	extended	flexed		TOP at 21 weeks
21	talipes at 21 weeks	21	talipes	extended	flexed	micrognathia	TOP at 24 weeks
22	talipes at 22 weeks	22	talipes	flexed	flexed	micrognathia	TOP at 22 weeks
23	talipes at 24 weeks	24	talipes	extended	flexed	micrognathia	TOP at 24 weeks
24	talipes at 24 weeks	24	talipes	extended	flexed	nuchal edema, pleural effusions	IUD at 27 weeks
25	polyhydramnios at 27 weeks	27	talipes	flexed	flexed	ascites, pleural effusions, skin edema	TOP at 28 weeks
26	polyhydramnios at 27 weeks	27	talipes	flexed	flexed		NND at 29 weeks
27	polyhydramnios at 28 weeks	28	talipes	extended	flexed	ascites, pleural effusions, skin edema, micrognathia	NND at 33 weeks
28	polyhydramnios at 30 weeks	30	talipes	extended	flexed	micrognathia	NND at 32 weeks
29	polyhydramnios at 31 weeks	31	talipes	extended	flexed	collapsed stomach	IUD at 32 weeks
30	polyhydramnios at 31 weeks	31	talipes	extended	flexed	pleural effusions, hydronephrosis	NND at 36 weeks
31	polyhydramnios at 34 weeks	34	talipes	extended	flexed	collapsed stomach	IUD at 35 weeks
32	polyhydramnios at 34 weeks	34	talipes	flexed	flexed	micrognathia, collapsed stomach, hydronephrosis	NND at 36 weeks

TOP, termination of pregnancy; IUD, intrauterine death; NND, neonatal death; *the same patient in two consecutive pregnancies

micrognathia, three (11%) had ventriculomegaly, six (22%) had hydronephrosis and six (22%) had 'collapsed' stomach in association with polyhydramnios. There were 16 terminations of pregnancy at the request of the parents, five intrauterine deaths and six neonatal deaths.

DISCUSSION

The data of this study on the ultrasonographic findings in lethal arthrogryposis during the second and third trimesters of pregnancy are compatible with those of previous reports[4,8]. In all cases there was talipes with flexion deformities of the wrists and elbows and either flexion or extension of the knees. However, as illustrated by the findings in the group of patients with a previous history of arthrogryposis, it is important that serial ultrasound examinations are carried out, because the talipes and other joint deformities may not become apparent until 27 weeks of gestation. Micrognathia, which is also a common finding in fetuses with lethal arthrogryposis, is thought to be the consequence of neuromuscular dysfunction, since fetal muscle movement is required for the normal integrated growth of the craniofacial bones[1].

Polyhydramnios, presumably due to impaired swallowing, which can also account for the 'collapsed' stomach, was present in about 20% of our cases and this was found after 26 weeks of gestation. This late-onset polyhydramnios, which is characteristic of all conditions that interfere with fetal swallowing, such as anencephaly, diaphragmatic hernia and esophageal, duodenal or ileal atresia, presumably reflects the fact that, with advancing gestation, fetal swallowing plays an increasingly important role in the regulation of amniotic fluid volume.

In those cases that were examined at 10–14 weeks of gestation, increased nuchal translucency thickness was present in both fetuses with arthrogryposis, whereas the translucency was normal in the three fetuses that were subsequently found to be normal. In a previous ultrasonographic study of lethal arthrogryposis, all five affected fetuses that were examined at 15–16 weeks of gestation had subcutaneous edema[4]. In our study of 27 affected fetuses that were examined after 16 weeks of gestation, nuchal edema was present in about one-quarter of the cases.

Since lethal arthrogryposis is a heterogeneous condition, it is possible that abnormal accumulation of nuchal fluid is found in only some of the cases. Alternatively, as with chromosomal abnormalities such as trisomies 21, 18 and 13, Turner's syndrome and triploidy, increased nuchal translucency at 10–14 weeks may be a common transient feature found in the majority of fetuses with arthrogryposis, irrespective of whether the underlying defect is neurogenic, muscular or connective tissue-related. In this respect, it is of interest that both fetuses with arthrogryposis presenting with increased nuchal translucency thickness had narrowing of the aortic isthmus, which is a common finding in chromosomally abnormal fetuses with increased translucency[9].

Prenatal diagnosis of lethal arthrogryposis is based on the demonstration of multiple joint contractures that may not become apparent until the end of the second trimester of pregnancy. However, at least in some cases, the condition may present as increased nuchal translucency thickness at 10–14 weeks of gestation.

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