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Increased nuchal translucency thickness at 10–14 weeks of gestation as a predictor of severe twin-to-twin transfusion syndrome

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ABSTRACT

This study examines a possible association between increased nuchal translucency thickness at 10–14 weeks of gestation in monochorionic twin pregnancies and the subsequent development of severe twin-to-twin transfusion syndrome (TTS). In 132 monochorionic twin pregnancies, including 16 that developed severe TTS at 15–22 weeks of gestation and 116 that did not develop TTS, crown–rump length, nuchal translucency thickness and fetal heart rate were measured at 10–14 weeks. In those that developed severe TTS, the prevalence of nuchal translucency thickness above the 95th centile of the normal range and the inter-twin difference in nuchal translucency thickness and fetal heart rate were significantly higher than in the non-TTS group; there were no significant differences between the groups in the inter-twin difference in crown–rump length. For fetal nuchal translucency above the 95th centile, the positive and negative predictive values for the development of TTS were 38% and 91%, respectively; the likelihood ratios of nuchal translucency above or below the 95th centile for the development of severe TTS were 4.4 (1.8–9.7) and 0.7 (0.4–0.9), respectively. These findings demonstrate that the underlying hemodynamic changes associated with TTS may manifest as increased fetal nuchal translucency thickness at 10–14 weeks of gestation.

INTRODUCTION

In dichorionic twin pregnancies at 10–14 weeks of gestation, the prevalence of nuchal translucency thickness above the 95th centile of the normal range is similar to that in singleton pregnancies. In a study of 344 such pregnancies, increased translucency was observed in 37 of the 688 fetuses (5.4%) or in at least one fetus in 9.0% of the pregnancies; in contrast, increased translucency was detected in at least one fetus in 13.7% of 95 monochorionic pregnancies[1].

In singleton pregnancies, there is a strong association between increased fetal nuchal translucency thickness and chromosomal defects[2,3]. Since in monochorionic twins there is no evidence of increased prevalence of chromosomal defects, we postulated that the high prevalence of increased nuchal translucency may be an early manifestation of the circulatory imbalance associated with twin-to-twin transfusion syndrome (TTS). Certainly, in singleton pregnancies, there is evidence that, in both chromosomally abnormal and normal fetuses, one of the possible mechanisms of increased translucency is cardiac dysfunction[4,5].

The aim of this study was to examine a possible association between increased nuchal translucency thickness at 10–14 weeks and the subsequent development of severe TTS.

METHODS

At the Harris Birthright Research Centre for Fetal Medicine, there is an ongoing screening study for chromosomal abnormalities by a combination of maternal age and fetal nuchal translucency thickness at 10–14 weeks of gestation[3]. Transabdominal ultrasound examination is carried out to obtain a sagittal section of the fetus for measurement of the crown–rump length and nuchal translucency thickness. Simultaneous M-mode and real-time B-mode imaging are used to obtain recordings of six to eight fetal cardiac cycles, the interval is measured with electronic calipers and the heart rate is calculated using the software of the ultrasound machine. Twin pregnancies are classified as dichorionic if the placentae are not adjacent to each other, or if, in the presence of a single placental mass, there is extension of placental tissue into the base of the intertwin membrane (lambda sign)[6]. In monochorionic pregnancies, there is a single placental mass in the absence of the lambda sign[7]. In twin pregnancies, gestational age is calculated on

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the basis of the crown–rump length of the largest fetus. Demographic details and ultrasound findings are entered into a computer database at the time of scanning. Pregnancy outcome is obtained from the maternity units or the patients themselves.

A computer search was made for monochorionic twin pregnancies with live fetuses at 10–14 weeks of gestation and an estimated date of delivery before 1 January 1997. The pregnancies were subdivided into those that developed severe TTS and those that did not develop this pregnancy complication and the two groups were compared for fetal crown–rump length, nuchal translucency thickness and fetal heart rate. For the purposes of this study, severe TTS was defined by the development of acute polyhydramnios at less than 24 weeks of gestation and the ultrasonographic features of anhydramnios and non-visible bladder in the donor fetus in combination with polyhydramnios and a dilated bladder in the recipient fetus, which resulted in either miscarriage or fetal death, or required intrauterine treatment.

The χ^2 test was used to determine the significance of differences between the two groups in the proportion with measurements of nuchal translucency thickness and/or fetal heart rate above the 95th centile of the normal range for singletons[8,9]. In addition, the Mann–Whitney *U* test was used to compare the groups for demographic details and inter-twin differences in fetal crown–rump length, nuchal translucency thickness and fetal heart rate.

RESULTS

During a 4-year period (1993–96), we examined 143 monochorionic twin pregnancies with live fetuses at 10–14 weeks of gestation. In six of the pregnancies, one of the fetuses had a severe abnormality, including three with anencephaly, and one case each with severe kyphoscoliosis, obstructive uropathy and anencephaly with acardia; these cases were excluded from further analysis. Also excluded were five pregnancies resulting in unexplained mid-trimester miscarriage or intrauterine death of one or both of the fetuses. There were no cases of chromosomal abnormalities.

In the remaining 132 pregnancies, there were 16 with severe TTS and 116 without this complication. In the 16 with TTS, there were 11 that were treated with endoscopic laser coagulation of the communicating vessels at 15–22 weeks of gestation; eight of these resulted in live births and three were associated with miscarriage or intrauterine death of both fetuses. At the time of endoscopic surgery, none of the fetuses had sonographic evidence of hydrops fetalis or increased nuchal fold thickness. In the other five pregnancies with severe TTS, no treatment was undertaken, but there was mid-trimester miscarriage or intrauterine death of both fetuses within 2 weeks of an ultrasound examination that demonstrated features of developing TTS. There were no other pregnancies resulting in miscarriage or perinatal death.

The crown–rump length and nuchal translucency thickness were measured in all 132 cases, but the fetal heart rate was measured only in the last 92 cases. There were no significant differences between those pregnancies that developed severe TTS and those that did not, in the median maternal age, parity, gestation at the 10–14-week scan or inter-twin difference in crown–rump length (Table 1). However, in the severe TTS group, both the prevalence of nuchal translucency thickness and fetal heart rate above the 95th centile of the normal range for singletons[8,9] and the inter-twin difference in nuchal translucency thickness and fetal heart rate were significantly higher than in the non-TTS group (Table 1, Figure 1). For fetal nuchal translucency above the 95th centile, the positive and negative predictive values for the development of TTS were 38% and 91%, respectively; the likelihood ratios of nuchal translucency above or below the 95th centile for the development of TTS were 4.4 (1.8–9.7) and 0.7 (0.4–0.9), respectively.

DISCUSSION

All monochorionic twin pregnancies are characterized by the presence of vascular anastamoses between the two fetoplacental circulations[10], but a circulatory imbalance resulting in the development of acute second-trimester polyhydramnios is present in only about 10–20% of the cases[11]. The findings of this study suggest that ultrasonographic

Table 1 Comparison of demographic characteristics and findings of the ultrasound examination at 10–14 weeks of gestation in 132 monochorionic twin pregnancies. The values given are the median and range. NT > 95th centile, pregnancies in which the nuchal translucency (NT) thickness of at least one fetus was above the 95th centile of the normal range for singletons; FHR > 95th centile, pregnancies in which the fetal heart rate (FHR) of at least one fetus was above the 95th centile of the normal range for singletons

	Severe TTS (*n* = 16)	*Non-TTS* (*n* = 116)	*p value*	*Median difference (95% CI)*
Maternal age (years)	31 (22–41)	33 (19–44)	NS	−1 (−5 to 2)
Parity	1 (0–4)	1 (0–8)	NS	0 (−1 to 1)
Gestation (weeks)	13 (11–14)	12 (11–14)	NS	0 (0 to 1)
CRL difference (mm)	3 (1–16)	3 (0–16)	NS	0 (−1 to 1)
NT difference (mm)	0.7 (0.1–4.0)	0.2 (0–5.5)	< 0.001	0.5 (0.2 to 0.8)
FHR difference (bpm)	8 (0–14)	4 (0–25)	< 0.05	4 (0 to 7)
NT > 95th centile	6/16 (37.5%)	10/116 (8.6%)	< 0.001	χ^2 = 11.0
FHR > 95th centile	1/11 (9.1%)	6/81 (7.4%)	NS	χ^2 = 0.04

TTS, twin-to-twin transfusion syndrome; CRL, crown–rump length; NS, not significant

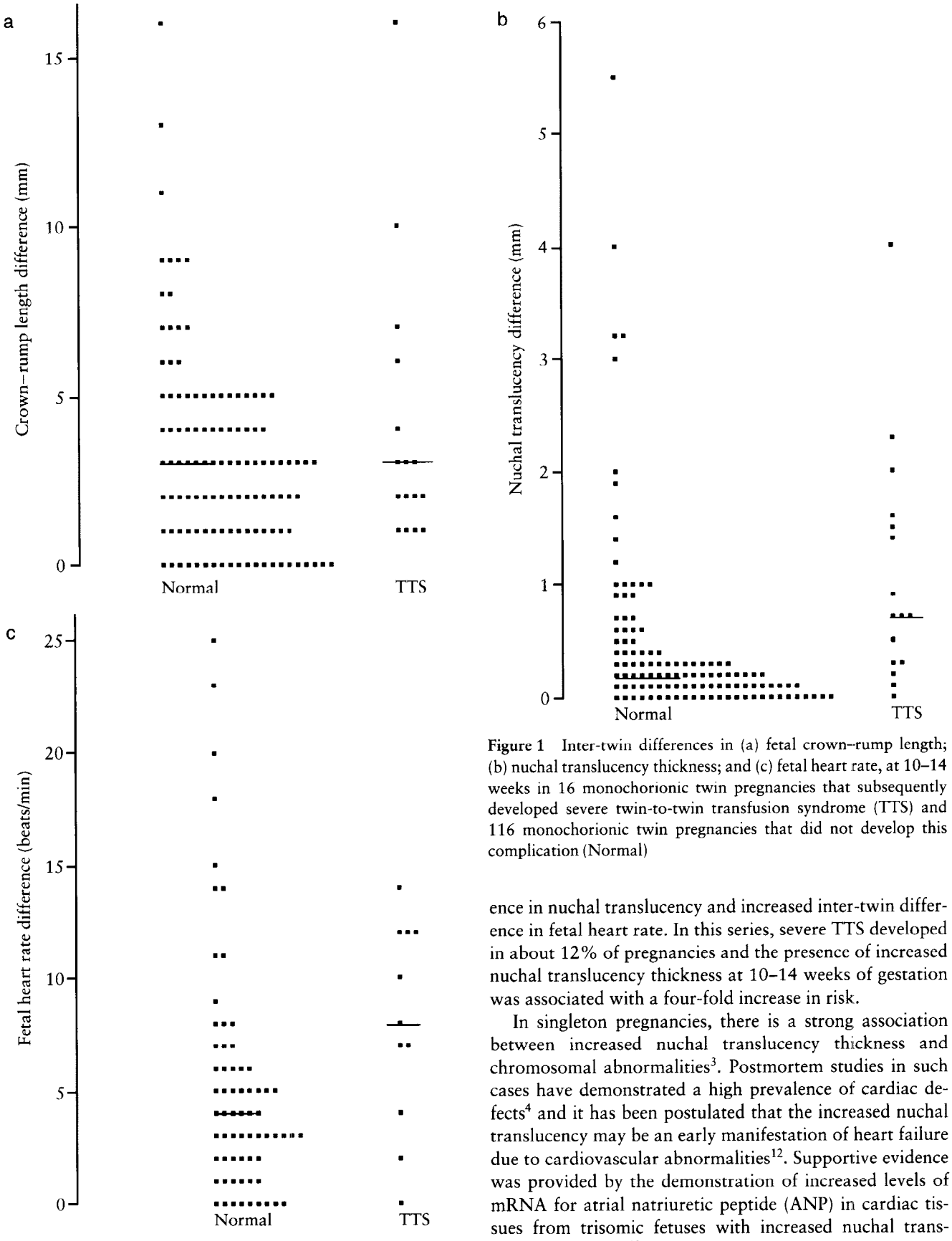

Figure 1 Inter-twin differences in (a) fetal crown–rump length; (b) nuchal translucency thickness; and (c) fetal heart rate, at 10–14 weeks in 16 monochorionic twin pregnancies that subsequently developed severe twin-to-twin transfusion syndrome (TTS) and 116 monochorionic twin pregnancies that did not develop this complication (Normal)

features of the underlying hemodynamic changes in severe TTS may be present from as early as 10–14 weeks of gestation and manifest as increased nuchal translucency thickness in one of the fetuses, increased inter-twin difference in nuchal translucency and increased inter-twin difference in fetal heart rate. In this series, severe TTS developed in about 12% of pregnancies and the presence of increased nuchal translucency thickness at 10–14 weeks of gestation was associated with a four-fold increase in risk.

In singleton pregnancies, there is a strong association between increased nuchal translucency thickness and chromosomal abnormalities[3]. Postmortem studies in such cases have demonstrated a high prevalence of cardiac defects[4] and it has been postulated that the increased nuchal translucency may be an early manifestation of heart failure due to cardiovascular abnormalities[12]. Supportive evidence was provided by the demonstration of increased levels of mRNA for atrial natriuretic peptide (ANP) in cardiac tissues from trisomic fetuses with increased nuchal translucency thickness[12]. It is possible that, in monochorionic twin pregnancies, increased nuchal translucency thickness in the recipient fetus may also be a manifestation of heart failure due to hypervolemic congestion. Although in such cases, as in trisomic fetuses, there may be increased cardiac

production of ANP, the appropriate receptors or response in the kidney may not be sufficiently developed by 10–14 weeks of gestation. Consequently, the recipient fetus may demonstrate transient congestive heart failure which resolves with advancing gestation and the development of diuresis that would tend to correct the hypervolemia and reduce heart strain. In this respect, it is of interest that, in our cases with severe TTS resulting in polyhydramnios at 15–22 weeks of gestation, the fetuses did not have sonographically detectable nuchal edema.

In fetuses from monochorionic twin pregnancies, the prevalence of increased nuchal translucency thickness is higher than in singletons and in dichorionic twins[1]. The findings of this study suggest that one possible factor contributing to this increased prevalence is the circulatory imbalance associated with twin-to-twin transfusion syndrome. Consequently, the presence of increased nuchal translucency thickness in monochorionic twins at 10–14 weeks should stimulate the sonographer to undertake close surveillance for early diagnosis of the clinical features of severe twin-to-twin transfusion syndrome. The extent to which such an earlier diagnosis would lead to therapeutic interventions with higher survival remains to be determined.

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