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Ultrasound screening for anencephaly at 10–14 weeks of gestation

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ABSTRACT

In an ongoing study involving seven hospitals in London and surrounding areas, 55 237 fetuses were examined by ultrasound at 10–14 weeks of gestation. There were 47 fetuses (1 in 1175) with anencephaly which presented with acrania with varying degrees of cerebral degeneration. The first audit of results was performed in April 1995. During the first phase of the study 34 830 fetuses were examined and in eight of the 31 with anencephaly the diagnosis was not made at the 10–14-week scan. Following the audit, 20 407 fetuses were examined and in all 16 with anencephaly the diagnosis was made at the 10–14-week scan (p = 0.03). These findings demonstrate that anencephaly can be reliably diagnosed at the routine 10–14-week ultrasound scan, provided a specific search is made for the sonographic features for this condition.

INTRODUCTION

Prenatal ultrasonographic diagnosis of anencephaly during the second and third trimesters of pregnancy, which is based on the demonstration of absent cranial vault and cerebral hemispheres, has been possible for more than 20 years[1]. Animal studies and studies in humans have reported that the primary defect is absence of the cranial vault, with subsequent disruption of the cerebral cortex, leading to anencephaly[2–4]. Since in normal fetuses mineralization of the skull, and therefore hyperechogenicity in comparison to the underlying tissues, occurs at around the 10th week of gestation[5], diagnosis of anencephaly by ultrasound is theoretically possible from this gestational age onwards.

The aim of this multicenter screening study was to determine the prevalence of anencephaly and the sensitivity of ultrasound diagnosis for this condition at 10–14 weeks of gestation.

PATIENTS AND METHODS

During a 3-year period (September 1992–January 1996), 54 336 women with live fetuses, including 901 twin pregnancies, took part in an ultrasound study to determine the effectiveness of screening for chromosomal abnormalities by assessment of fetal nuchal translucency thickness at 10–14 weeks of gestation[6,7]. In 28 891 fetuses, the ultrasound scan was performed as part of routine antenatal care in any one of seven district general hospitals (Basildon Hospital, Basildon; Heatherwood Hospital, Ascot; King's College Hospital, London; Frimley Park Hospital, Camberley; Princess Royal Hospital, Haywards Heath; Queen Mary's Hospital, Sidcup and St. Peter's Hospital, Chertsey). In 26 346 fetuses, the scan was carried out on self-referred women at the Harris Birthright Research Centre for Fetal Medicine, London.

Transabdominal ultrasound examination was performed at 10–14 weeks of gestation for measurement of the fetal crown–rump length and nuchal translucency thickness. In addition, data on any obvious fetal abnormalities were recorded and demographic details and the findings of the ultrasound examinations were entered into a computer database at the time of the scan. A further scan was carried out at 18–22 weeks for detailed examination of fetal anatomy. Data on pregnancy outcome were obtained from the patients themselves or their hospitals.

The first audit of results was carried out in April 1995 and, following this, the sonographers from the participating centers were informed of the different diagnostic features of anencephaly in the first compared to the second trimester and they were instructed to specifically look for and record the presence or absence of acrania at the 10–14-week scan. In all cases, diagnosis of anencephaly at 10–14 weeks was confirmed by a second scan at a specialist center.

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The prevalence of anencephaly was determined by combining data from first- or second-trimester ultrasound examination and the findings at birth. The sensitivity of the 10–14-week scan in the diagnosis of anencephaly was examined before and after the first audit of results and the significance of differences in detection rate between the two period-groups was determined by the Fisher exact test.

For cases where women had regular menstrual cycles and were certain of the date of their last menstrual period, the crown–rump length of fetuses with anencephaly was expressed as the number of standard deviations by which it differed from the normal mean for gestation (delta value)[8]. The significance of differences between crown–rump length in normal and anencephalic fetuses was examined using Student's t test and the relationship of the difference with gestation examined using regression analysis.

RESULTS

The mean gestational age at the first scan was 12 weeks (range 10–14 weeks). There were 47 fetuses with anencephaly, including three from twin pregnancies, giving a prevalence of 1 in 1175 fetuses. The diagnosis of anencephaly was made at the 10–14-week scan in 39 cases and at the 18–22-week scan in a further eight cases; there were no live births with anencephaly. In the first trimester, the pathognomonic feature was acrania, the brain being either entirely normal or at varying degrees of distortion and disruption (Figure 1). In the second trimester, in addition to acrania, there was absence of most of the brain.

At the time of the first audit of results (April 1995), first-trimester ultrasound examination had been carried out on 34 830 fetuses. In this group, there were 31 cases of anencephaly; in 23 (74.2%) cases the diagnosis of anencephaly was made at the 10–14-week scan and in eight cases at the 18–22-week scan. In the second phase of the study, 20 407 fetuses were examined and all 16 cases of anencephaly were diagnosed at the 10–14-week scan ($\chi^2 = 5.0$, $p = 0.03$).

In 37 of the 47 cases of anencephaly, the mothers had regular menstrual cycles and were certain of the date of their last menstrual period. In ten (27%) of the 37 cases, the fetal crown–rump length was below the 5th centile of the normal range for gestational age (Figure 2). The mean fetal crown–rump length was significantly lower than the expected normal mean for gestation (mean difference = −1.01 SD, $t = 4.6$, $p < 0.0001$) and this deviation from normality increased with gestation ($r = -0.44$, $p < 0.01$).

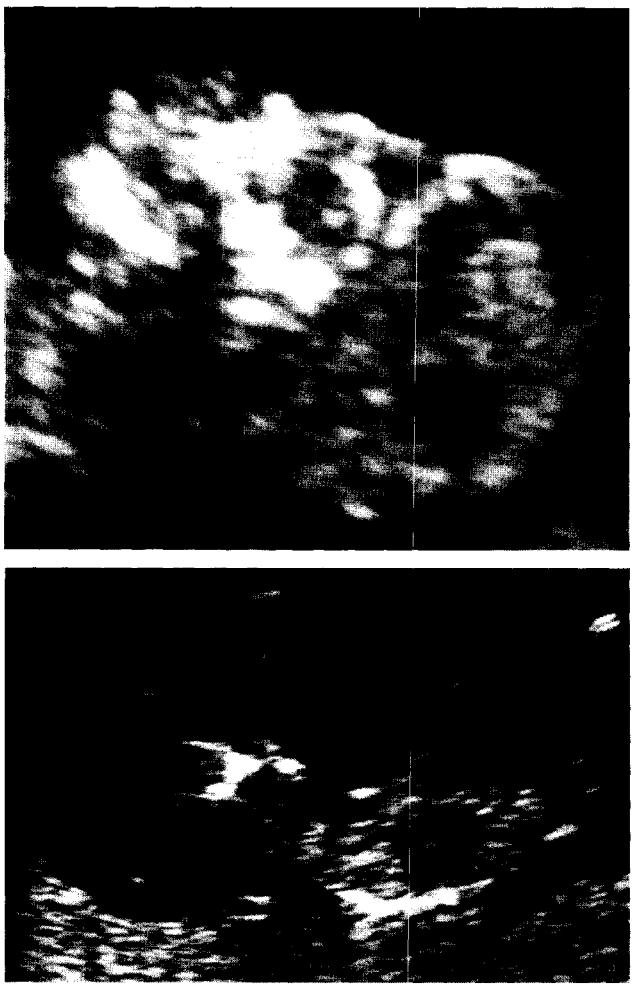

Figure 1 In anencephaly, ultrasound examination at 10–14 weeks of gestation may demonstrate acrania with either a normal looking brain (above), or a distorted degenerating brain (below)

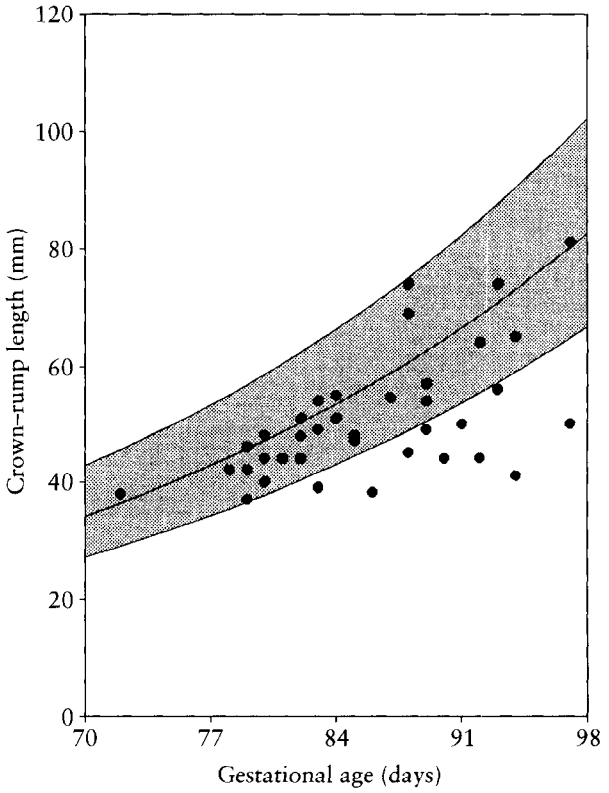

Figure 2 The fetal crown–rump length in the majority of fetuses with anencephaly at 10–14 weeks of gestation is within the normal range (mean, 5th and 95th centiles shown), but, with advancing gestation and increasing degeneration of the brain, the crown–rump length is decreased

DISCUSSION

This study demonstrates the value of audit in improving a clinical service. Through audit it was possible to identify that, in a high proportion of fetal anencephaly, there is failure to diagnose the condition at the routine 10–14-week scan. It was hypothesized that the most likely reason for this failure was that, at the 10–14 week scan, the only sonographic feature may be acrania, unlike the easily detectable absence of the cerebral hemispheres as well as the cranial vault at the 18–22-week scan. Subsequent instruction of the ultrasonographers as to this difference in the phenotype of anencephaly at different gestational ages, and requests that they specifically search for acrania at the 10–14-week scan, resulted in improved diagnosis. This was achieved without the need to increase resources.

In the group of anencephalic fetuses, the mean fetal crown–rump length was significantly reduced but the crown–rump length was below the 5th centile of the normal range in only 27% of the cases. This is not surprising since in the majority of cases the only sonographic abnormality in early pregnancy is acrania. However, with advancing gestation, there is progressive degeneration of the fetal brain with consequent reduction in crown–rump length.

Traditionally, prenatal diagnosis of anencephaly was made by amniocentesis in patients with high maternal serum α-fetoprotein at 16 weeks of gestation[9], and more recently by ultrasound examination at 20 weeks[10,11]. This study has demonstrated the feasibility of first-trimester diagnosis by ultrasonography. The obvious advantage of early diagnosis is the option for less traumatic termination of pregnancy. A potential criticism of early compared to late diagnosis of a highly lethal abnormality is that in some cases there would be spontaneous miscarriage, removing the need for prenatal diagnosis and elective abortion. However, in such cases, the parents will not receive adequate counselling that their risk of recurrence of a neural tube defect has effectively increased from about 1 to 50 in 1000.

Since the prevalence of fetal anencephaly is around 1 in 1200 pregnancies, in any one maternity unit there would be only 2–4 cases, per year and therefore meaningful audit can only be achieved by examining data from well co-ordinated multicenter studies. The results of this study demonstrate how data can be obtained from the creation of a network of centers working with common protocols.

The early pregnancy scan was initially introduced with the primary intention of pregnancy dating. Subsequently, a series of studies have demonstrated that, during this scan, the fetal nuchal translucency can be measured and this measurement may provide an effective method of screening for chromosomal defects[6,7]. The aim of setting up the multicenter study was to examine the sensitivity and specificity of screening for trisomy 21 by fetal nuchal translucency thickness. However, it soon became obvious that, with the 10–14-week scan, it was possible to diagnose an increasing number of fetal abnormalities. As demonstrated in this study on anencephaly, through the use of audit it was possible to investigate and subsequently improve the sensitivity of the scan in the early diagnosis of this lethal abnormality. The same structure and process can now be used to examine the value of the early scan in the diagnosis of a wide range of other fetal defects.

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