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Examination of fetuses after induced abortion for fetal abnormality

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Abstract

***Objective*—To determine the accuracy of midtrimester diagnosis of fetal abnormality by examination and investigation of fetuses after induced abortion.**

***Design*—Prospective study over five years of fetuses aborted in the midtrimester because of abnormalities detected by ultrasonography and amniocentesis. Techniques included a full external examination by a clinical geneticist with experience in dysmorphology and other investigations including necropsy.**

***Setting*—Regional genetic centre.**

***Participants*—Clinicians working within the North Western region who wished to use the service offered.**

***Results*—133 Fetuses were aborted because of abnormalities detected on ultrasonography and 115 because of abnormal findings on amniotic fluid analysis. In a further two cases fetal abnormality was diagnosed by molecular genetic and biochemical techniques. Among the fetuses with abnormal scans the pretermination diagnosis was changed or refined in a way which affected genetic counselling in 53 of 133 cases. Among the 115 fetuses diagnosed as abnormal by amniocentesis the pretermination diagnosis was confirmed in 112 cases and altered in three.**

***Conclusion*—Fetuses aborted because of abnormalities detected by screening should be examined by suitably experienced clinicians, both for accurate genetic counselling of the families and for quality control of the tests employed.**

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TABLE I—*Routine observations on each midtrimester fetus*

Fetus	Placenta
Weight	Weight
Crown-rump length and crown-heel length	Macroscopic appearance
Occipitofrontal circumference	Number of cord vessels
Foot length, medial border	Length of cord
Inner and outer canthal distance	
External sex	
External appearance documenting structural abnormalities	

TABLE II—*Investigations performed on midtrimester fetuses*

Investigation	Indication
Photographs using good quality, slow speed film	To provide permanent record for future reference. Parents may ask to see a photograph at later stage
Chromosome analysis from: (*a* Fetal blood (*b*) Skin and muscle biopsy samples (*c*) Amnion (*d*) Umbilical cord (*e*) Placenta	Suspected chromosome abnormality in fetus; fetal membranes may grow even if fetus is macerated. To check for chromosome abnormality confined to placenta
Virological, bacteriological studies	If infective aetiology is suspected—for example, cytomegalovirus, parvovirus
Metabolic studies from fetal blood or tissue	Suspected metabolic disorder—for example, Gaucher's disease
Radiological investigations	If skeletal dysplasia is suspected
DNA analysis from blood or tissue	To confirm diagnosis if there is specific gene probe or deletion, or to use for family studies in future pregnancy. Storage

Introduction

An ultrasound scan in the midtrimester is now a routine part of antenatal care in most maternity hospitals. As technology improves and skill increases more fetal abnormalities are being recognised in the scans.[1] The number of amniocenteses performed also continues to rise, mainly as a result of chromosomal screening for high maternal age. These two types of screening procedure can detect serious fetal abnormalities and some parents will opt for termination of the pregnancy.[2] In the North Western region we offer a service to examine fetuses aborted after a diagnosis of fetal abnormality. Many clinicians use the service but this study does not represent complete ascertainment, though virtually all fetuses aborted after amniocentesis diagnosis in the department are examined. We examined 250 fetuses aborted over five years because of abnormalities detected in the midtrimester and found that the pretermination diagnosis could often be changed or altered substantially in a way which affected genetic counselling. This paper summarises our findings.

Subjects and methods

Two hundred and fifty fetuses which had been aborted in the midtrimester because of fetal abnormality were received into the regional genetic centre over the five years 1982-7. In 115 cases the diagnosis had been made on amniocentesis samples and a further 133 fetuses had major abnormalities detected by ultrasonography. One fetus was aborted because of maternal phenylketonuria, and one was at high risk of carrying the gene for Huntington's chorea. All referring doctors were asked to give the pretermination diagnosis and to state by which method this had been made. Throughout this report the pretermination diagnosis is taken to be that on which the parents and obstetrician acted when deciding on termination of pregnancy. We request that fetuses are sent as soon after termination as possible in a dry, clean container. Table I lists the routine observations made in each case.

When noting the external appearance we take postmortem changes into account, as these may be mistaken for anomalies and may alter some measure-

ments appreciably, particularly the occipitofrontal circumference. Medial foot length gives the best correlation with gestational age of all the parameters measured.[3] Some features such as ear positioning and size of genitalia differ in midtrimester fetuses compared with term neonates and it is important that the examiner is aware of this. Findings on examination may suggest the need for further investigations, and these are listed in table II.

TABLE III—*Fetal diagnoses before and after termination and alterations in counselling*

Diagnosis before termination	No of cases	Diagnosis after termination	No of cases	Modified diagnosis with no change in risk (C), increased risk (C+), decreased risk (C−)
		Terminations after ultrasonography		
Neural tube defect	71	Isolated neural tube defect	56	
		Neural tube defect and cleft palate	2	
		Neural tube defect and multiple congenital anomalies (unknown cause)	5	C+
		Likely autosomal recessive malformation syndrome	3	C+
		Autosomal recessive cystic hygroma[1]	1	C+
		45,X karyotype	3	C−
		Early amnion rupture	1	C−
Structural brain defect (hydrocephalus (5 cases), absent corpus callosum (1), odd shaped head (2), abnormal ventricles (1), microcephaly (1))	10	Isolated defect confirmed	5	
		Early amnion rupture	2	C−
		Hydrolethalus syndrome[2]	1	C+
		Meckel-Gruber syndrome[3]	1	C+
		Cebocephaly	1	C+
Abdominal wall defect	11	Gastroschisis	4	
		Exomphalos	1	
		Exomphalos and diaphragmatic hernia	1	C
		Exomphalos and de novo t(Y:15)	1	C−
		Early urethral obstruction	1	C
		Early urethral obstruction with trisomy 18	1	C+
		Imperforate anus	1	C
		OEIS complex[4]	1	C
Fetal hydrops	11	45,X	6	C−
		Trisomy 21	1	C+
		Twin/twin transfusion	1	C−
		Short limbed dwarf	1	C+
		No cause identified, 46,XX	2	
Known syndrome (previous family history)	7	Meckel-Gruber syndrome[3]	3	
		Osteogenesis imperfecta type IIB	1	
		Autosomal recessive polycystic kidneys	1	
		Autosomal recessive multiple congenital anomalies syndrome	1	
		Treacher Collins syndrome[5]	1	
Placental abnormality	4	Triploidy	3	C−
		Translocation trisomy 13 with paternal t(13:14)	1	C+
Cardiac defect	1	9p Tetrasomy	1	C−
Short limbs	2	Achondrogenesis	1	C+
		Osteogenesis imperfecta type IIB	1	C+
Renal agenesis	2	Isolated renal agenesis	2	
Severe growth failure	3	Triploidy	1	C+
		Microcephaly and joint contracture syndrome (likely autosomal recessive)	1	C+
		No cause identified	1	
"Abnormal"	11	Early amnion rupture	3	C−
		Body stalk anomaly	3	C−
		Early urethral obstruction and trisomy 13	1	C+
		Renal cystic dysplasia	3	C+
		Multiple congenital anomalies syndrome	1	C+
Total	133		133	C=4 C+=25 C−=24
		Terminations after amniocentesis		
Chromosome abnormality	71	Trisomy 21	39	
		Trisomy 21 mosaic	1	
		Trisomy 13	5	
		Trisomy 18	11	
		Sex chromosome aneuploidy	5	
		69,XXX	1	
		Unbalanced translocation	4	
		De novo translocation	3	
		+18, +8	1	
		Mosaic 5p-	1	
Neural tube defect	32	Anencephaly	8	
		Spina bifida	18	
		Neural tube defect and abdominal wall defect	3	
		Meckel-Gruber syndrome[3]	2	C+
		Multiple congenital anomalies with maternal t(2:7)	1	C+
Male fetus at risk of Duchenne's disease	6	Confirmed male	6	
Male fetus at risk of Becker's disease	1	Confirmed male	1	
Abdominal wall defect	4	Confirmed isolated abdominal wall defect	4	
α Thalassaemia	1	Confirmed	1	
Total	115		115	C=0 C+=3 C−=0

Samples for chromosome analysis are obtained by a sterile technique and set up in culture immediately. Macerated tissue is unsuitable. We find that placental tissue grows well and can be used to differentiate between karyotypic abnormalities confined to the placenta and those present in both fetus and placenta. If examination of the fetus leads to suspicion of a particular diagnosis the pathologist is alerted to the possibility of associated internal abnormalities.[4] An immediate report of the examination findings is sent to the referring doctor suggesting any investigations considered necessary on other family members. This is followed by a further report when the necropsy findings become available. A genetic counselling appointment is offered to parents when appropriate and with the consent of the doctors concerned in their care.

Results

Table III shows the diagnoses before and after induced abortion of fetuses with abnormalities detected by ultrasonography or amniocentesis and the way in which the refined diagnosis influenced subsequent counselling. For the 133 fetuses diagnosed by ultrasonography the pretermination diagnosis was confirmed in 80 cases and revised in 53. Of those diagnosed by amniocentesis the pretermination diagnosis was confirmed in 112 cases and revised in three. In all 71 cases in which a chromosome abnormality had been diagnosed the pretermination diagnosis was confirmed as correct. The fetus at risk because of maternal phenylketonuria and the fetus at high risk of carrying a gene for Huntington's chorea both had a normal external appearance.

Discussion

Our results indicate that when fetal abnormality has been detected by scanning the diagnosis can often be refined by post-termination examination in a way which substantially affects counselling. Revised information about the aetiology of the condition, risk of recurrence, and possibility of prenatal diagnosis in subsequent pregnancies may be provided for the parents. Communication of the post-termination diagnosis back to the diagnostic teams is an important aspect of quality control. A further reason for establishing the diagnosis is for psychological benefit to the parents, who having made a difficult decision to end a wanted pregnancy are reassured that there were valid reasons for choosing to do as they did.

A particular diagnostic group to which attention should be drawn is those fetuses with a pretermination diagnosis of neural tube defect on ultrasonography. Of the 71 instances in this series, 15 fetuses had a post-termination diagnosis other than an isolated neural tube defect. The risk of recurrence for the newly diagnosed disorder was as high as one in four in some cases whereas in other cases the risk was much lower than the 4% currently quoted for neural tube defect in the North Western region. The methods of diagnosing neural tube defects during the study period changed. In the earlier years most fetuses were diagnosed by amniocentesis and measurement of the amniotic fluid α fetoprotein concentration. In the last year most neural tube defects were diagnosed by ultrasonography after the finding of a raised maternal serum α fetoprotein concentration.

A 45,X karyotype was the commonest cause in our series for the appearance of fetal hydrops during the second trimester. These fetuses were so severely hydropic on examination that survival to term would have been unlikely. The finding of a large, hydropic placenta indicated a chromosome abnormality in all cases seen.

Manchester *et al* from Denver reported a series of 257 pregnancies which were complicated by suspected fetal abnormality on ultrasonography.[1] Thirty seven per cent of the infants born had additional anomalies not detected by prenatal ultrasonography, and the authors concluded that prenatal diagnoses based on ultrasonography were remarkably accurate but were insensitive to associated anomalies in individual cases. Our study confirms this, a revised diagnosis being made in 53 (40%) of such cases.

We believe that examination of midtrimester fetuses by a clinical geneticist is a worthwhile service and improves diagnosis, which in turn benefits the diagnostic teams and parental counselling. It is best carried out by a clinician experienced in dysmorphology, used to normal variations in the appearance of fetuses at various stages in gestation, and familiar with rare dysmorphic syndromes. The collaboration of cytogeneticists and paediatric pathologists is important in defining the full extent of the anomalies in order to arrive at the final post-termination diagnosis, on which the parents will base their future reproductive decisions.

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Microalbuminuria as predictor of increased mortality in elderly people

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Abstract

***Objective*—Correlation of the urinary albumin excretion rate and the risk of death among elderly subjects.**

***Design*—216 Subjects aged 60-74 whose urinary albumin excretion rate had been determined were followed up 62-83 months later.**

***Setting*—Municipality of Fredericia, Denmark.**

***Subjects*—223 People who had been selected as control subjects for diabetics found during a systematic screening for diabetes of all people aged 60-74 living in the municipality of Fredericia, Denmark. Of these subjects, 216 had an extensive clinical and biochemical examination within a few weeks of selection.**

***Main outcome measure*—Death.**

***Results*—The median urinary albumin excretion rate was 7·52 μg/min. Eight of those with a rate below the median died compared with 23 with a rate equal to or greater than the median (p=0·0078). The median albumin excretion rate in the 31 who died was 15·00 μg/min. Cardiovascular disease was the most common cause of death in both groups. A multivariate regression analysis of survival data was performed using the proportional hazards model. Besides albumin excretion rate, male sex, serum creatinine concentration, and hypertension were found to be of prognostic value.**

***Conclusions*—The association between the albumin excretion rate and mortality that has been described in recent years in patients with diabetes mellitus may be present in elderly people in general, even when other known risk factors are taken into account.**

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Introduction

Excretion of urinary albumin above 20 μg/min (microalbuminuria)[1] is strongly prognostic of disease and death in diabetes mellitus.[2-8] The association between albumin excretion and the risk of death is also present when other risk factors such as male sex, age, obesity, ischaemic heart disease, hypertension, smoking, and raised blood lipid concentrations are taken into account.[1,3,5] Microalbuminuria is also associated with hypertension[9] and increased cardiovascular morbidity in people who are not diabetic.[5,10] We followed up a cohort of subjects drawn from the population of Fredericia[11] who were recruited to serve as controls for a cohort of diabetics aged 60-74 found during population screening. We followed up the subjects who were not diabetic for 62 to 83 months, or to death, and evaluated their urinary albumin excretion and other possible risk factors for death.

Subjects and methods

From 1 February 1981 to 31 October 1982 all people aged 60-74 living in the municipality of Fredericia, Denmark, were invited to have their blood glucose concentration measured after fasting overnight. The participants were also interviewed about a possible history of diabetes. Details of the sampling procedure and characteristics of those who did not respond have been described.[11] We invited 5699 people to participate, 5292 (92·9%) of whom accepted. Of these, 236 gave a history of diabetes. All the people screened were numbered consecutively, and for each diabetic subject a control was defined as the person with the nearest following number who was of the same sex and age (within one year) and whose fasting blood glucose concentration was below 7·0 mmol/l. Altogether 223 (94·5%) controls consented to further examination. Table I gives the age and sex distributions of this control group (the study population) and the corresponding total population of the municipality. All subjects were asked to have an extensive clinical and biochemical examination.

The blood and urine of subjects were sampled not later than three weeks after the initial screening. Venous blood obtained after subjects had fasted was tested for glucose, serum creatinine, triglyceride, total