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The surviving monozygotic twin

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SUMMARY It has been suggested that because of vascular interchange between the monozygous twins vascular disruptions from a deceased cotwin with disseminated intravascular coagulation causes embolisation in the surviving twin. This study reports six cases in which all the surviving monozygous twins had central nervous system infarcts and three had multiple organ infarcts, including pulmonary and hepatic infarcts, which have not been reported previously. Fetal death in utero occurred 1–11 weeks before the live birth of the monozygous survivor. In three cases there was pathological confirmation of a continuing process with infarcts ranging in age from a few days to eight weeks. Four infants died in the early neonatal period, and the remaining two survived with considerable handicap. A review of the published reports confirmed the high risk of vascular disruption affecting many organ systems and the extremely poor prognosis for subsequent death or handicap. We recommend that after detection of fetal death in utero in a suspected monozygous twin pregnancy careful consideration should be given to prompt delivery of the survivor and investigations should be carried out to rule out infarction in the central nervous system and other organs that are at risk.

The finding that 67% of twin pregnancies diagnosed by routine ultrasonography at 10 weeks' gestation turned out as singleton fetuses by the time of birth suggested that prenatal mortality in twins may occur with a higher than previously expected prevalence and that monozygotic twinning occurs more often than the observed 1 in 200 births.[1] The death of a cotwin in utero increases the risk of a vascular disruptive process, which results in disease in the surviving twin[2–17] because vascular interconnections between the twins commonly occur in monochorionic placentas. Monozygous twins are known to be at increased risk for structural defects.[3 15] This study reported the effects of fetal death in utero on six surviving and liveborn monozygous twins.

Patients and methods

After the admission of an index case all twin pregnancies with a known fetal death in utero before birth over a 10 year period were reviewed. For 14 such cases identified, placental disease was reviewed to determine the zygosity of the twins. Five additional cases were found to have diamnionic monochorionic placentation similar to that of the index case. This study reports on the six sets of monozygous twins where one twin died in utero and the surviving twin was subsequently liveborn.

Results

Report of the index case. A 32 year old gravida 2 woman with a previous miscarriage had a twin pregnancy diagnosed at 20 weeks' gestation by ultrasound. At 21 weeks she noted markedly decreased fetal movements and at 24 weeks a repeat ultrasound confirmed a fetal death in utero. At 26 weeks she had a small antepartum haemorrhage, which recurred at 28 weeks when an emergency caesarean section was performed because of fetal tachycardia. A 1170 g, appropriate weight for gestation male infant was delivered with an Apgar score of 2 at one minute and 5 at five minutes. His neonatal course was complicated by apnoea, which required mechanical ventilation, and hyperbilirubinaemia. Multifocal clonic seizures occurred at 7 hours of age, and cerebral ultrasonography at 11 hours showed large cysts in the parietal areas and periventricular haloes that suggested calcification (Fig. 1). The infant died at 80 hours of age. Necropsy findings confirmed bilateral parietal lobe infarction with calcification and cystic degeneration (Fig. 2). It also showed multiple thrombi in pulmonary arteries and old and recent hepatic infarcts. It was estimated from histological findings that the cerebral infarction was six weeks old, hepatic infarcts were two to four weeks old and one week

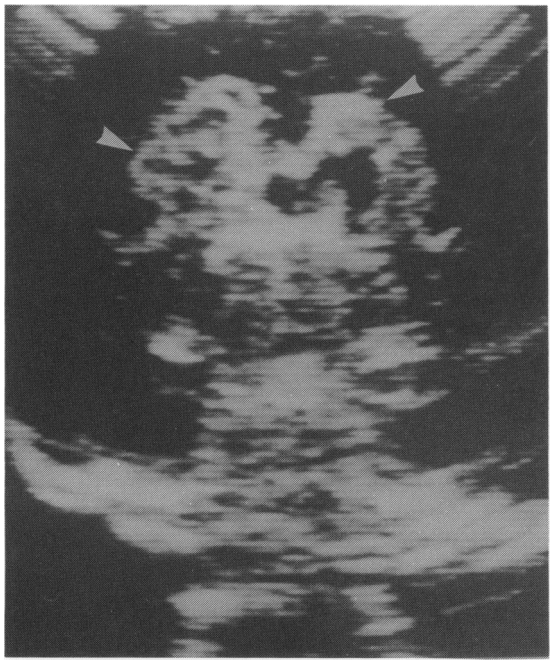

Fig. 1 *Cerebral ultrasound scan in index case. This shows periventricular echogenic haloes (arrows) with absence of echoes above this region (black area), suggesting sclerotic calcification and infarction of the parietal lobe.*

old, while pulmonary lesions were one to two weeks old.

Review of six cases. The clinical data of the six cases are summarised in Table 1. Fetal death in utero ranged from 1 to 11 weeks before the delivery of the surviving monozygous twin. No cause was found for the fetal death in utero in any instance. Four of the infants died in the early neonatal period, and the remaining two, who were alive at 3 and 5 years, respectively, have cerebral palsy and mental retardation. Table 2 shows the disease in the six cases diagnosed by obstetric ultrasound before birth, cerebral ultrasound or computerised tomographic scan after birth, and at necropsy in those who died.

Table 1 *Clinical data of the six cases*

Case No	*Gestation at fetal death in utero (wks)*	*Gestation of liveborn twin (wks)*	*Interval between fetal death in utero and birth (wks)*	*Outcome of liveborn twin*
1	21	28	7	Died at 4 days
2	20	31	11	Died at 2 hours
3	23	31	8	Died at 9 hours
4	26	32	6	Died at 1 hour
5	28	33	5	Survived handicapped
6	34	35	1	Survived handicapped

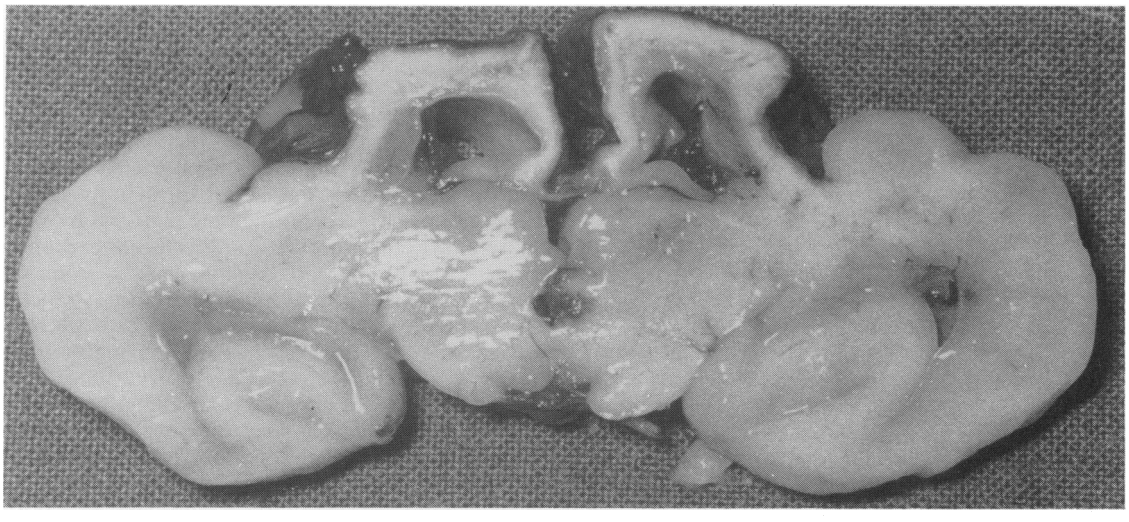

Fig. 2 *Brain disease in index case. Macroscopic section through the region of the central sulcus, showing bilateral symmetric necrosis of the parietal lobes and normal intact temporal lobes and basal ganglia.*

Table 2 *Data on disease in the surviving monozygous twin*

Case No	*Brain*	*Lung*	*Kidney*	*Spleen*	*Liver*
1	Parietal infarcts	Arterial thrombi	—	—	Multiple infarcts
2	Hydranencephaly	—	—	—	—
3	Occipital infarcts; hydrocephalus	Bilateral infarcts	Bilateral infarcts	Infarcts	—
4	Cerebellar infarcts	Bilateral infarcts	Cortical necrosis	Infarcts	—
5	Cortical infarcts	—	—	—	—
6	Parieto-occipital infarcts	—	—	—	—

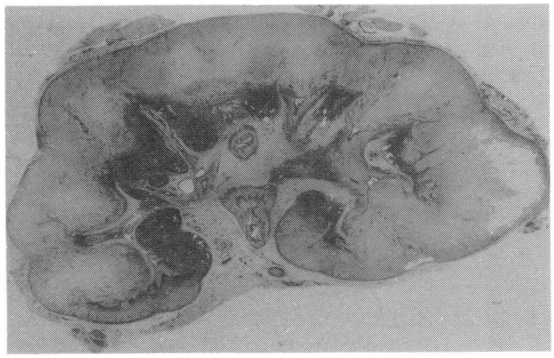

Fig. 3 *Renal disease in case 4. Haematoxylin and eosin stained section, showing pale areas of renal cortical necrosis and small amount of residual normal renal tissue (darker areas).*

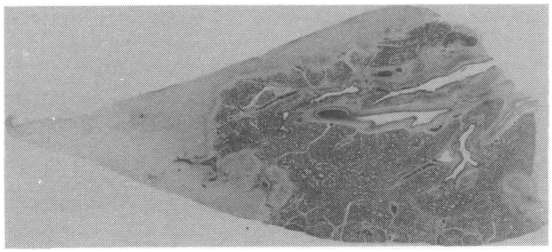

Fig. 4 *Lung disease in case 4. Haematoxylin and eosin stained section, showing pale areas of infarction, blood vessels occluded by recent thrombi, and residual normal pulmonary parenchyma (darker areas).*

All the infants had central nervous system damage, two had bilateral renal infarction (Fig. 3), two had bilateral pulmonary infarction (Fig. 4), two had splenic infarcts, and one had hepatic infarcts. Cases 1, 3, and 4 had evidence of an ongoing process with infarcts, which ranged from a few days to eight weeks. One of the long term survivors was also noted to have gross haematuria for two weeks; full renal investigations were not, however, undertaken.

Discussion

This retrospective study reported six cases where, following the fetal death in utero of the cotwin, the surviving monozygous twin was affected by vascular disruption of tissues secondary to embolic occlusion of vessels. A review of the published reports identified 16 previous reports and 47 cases published in the past 54 years. Cumulative data pooled from the total of 53 cases confirmed the relative risks of vascular disruption leading to disease in the central nervous system (72%), gastrointestinal system (including the liver and spleen) (19%), kidneys (15%), and lungs (8%) (Table 3). These findings were based on comprehensive necropsy examination of every organ system in most of the cases who died. In the remaining surviving infants a clinical and radiological diagnosis was made based on symptomatic involvement of the affected organs, with pathological confirmation in those who required surgical treatment. Pulmonary and hepatic infarcts found in the present series had not been previously reported. The nature of the damage depends on the timing of the fetal death in utero. Vascular disruption early in pregnancy leads to atresia or defects in organ development, while lesions such as arterial thrombosis or infarction develop when the pathological process occurs later in pregnancy.

Disruption of the central nervous system (CNS) is the most common complication reported in monozygous twin survivors. Vascular disruption by arterial occlusion has been confirmed on angiography[12] and at necropsy. Disruption can result in hydranencephaly, multicystic encephalomalacia, porencephaly, hydrocephalus, and focal cerebral or cerebellar infarcts. As severe cerebral damage leads to death or considerable handicap in the surviving monozygous twin the risk of subsequent occurrence is an important issue for parental counselling. In a review of 188 confirmed monozygous twin pairs seven cases of fetal death in utero occurred, and only two of these seven monozygous twin survivors had evidence of CNS disruption.[11] This gave an a priori risk of disruption leading to CNS damage of 0·5% in monozygous twins and an a priori risk of any

Table 3 *Systems affected in 53 liveborn monozygous twins. Cases in which a pathological diagnosis was made at necropsy or surgery are shown in brackets*

Reference	*Neurological*	*Gastrointestinal*	*Renal*	*Pulmonary*	*Others*	*None affected*
Brocher[2]	1 (1)	—	—	—	—	—
Confalonieri[3]	—	1 (1)	—	—	—	—
Bernirschke[4]	2 (2)	1 (1)	2	—	—	—
Reisman *et al*[5]	1 (1)	—	1 (1)	—	—	—
Moore *et al*[6]	2 (2)	2 (2)	3 (2)	1 (1)	—	—
Aicardi *et al*[7]	3 (1)	—	—	—	—	—
Saier *et al*[8]	—	1 (1)	—	—	—	—
Durkin *et al*[9]	5 (1)	—	—	—	—	—
Mannino *et al*[10]	—	—	—	—	2	—
Melnick[11]	1 (1)	—	—	—	—	6
Yoshioka *et al*[12]	3	—	—	—	—	—
Schinzel *et al*[13]	7 (5)	1 (1)	—	—	—	—
Hoyme *et al*[14]	1	1 (1)	—	—	—	—
Romero *et al*[15]	—	—	—	—	—	1
Jung *et al*[16]	6 (?)	—	—	—	—	—
Enbom[17]	—	—	—	—	—	2
Present report	6 (4)	3 (3)	2 (1)	3 (3)	—	—
Total	38	10	8	4	2	9
%	72	19	15	8	4	17

unborn twin pair exhibiting CNS damage due to vascular disruption of 0·16%.

The other organ systems affected in the surviving monozygous twin have led to diverse symptoms in the neonatal period. Intestinal atresia had led to abdominal distension and vomiting,[8 14] while renal cortical and medullary necrosis had led to haematuria, hypertension, renal failure, and death.[5 6] Pulmonary infarcts were the probable cause of respiratory distress in our two liveborn monozygous twins as no other lung disease was evident at necropsy.

A review of placentation in 250 twin pregnancies[4 18] first alerted obstetricians to the possibility of vascular anastomoses within a monochorionic placenta providing an access route to the circulation of the surviving twin. It was hypothesised that the death of a monozygous cotwin might predispose to disseminated intravascular coagulation and the generation of thromboplastin rich blood, which could in turn cause vascular disruption in the surviving twin. In our four cases studied at necropsy we found evidence of an ongoing process of vascular disruption in three infants. Histological findings showed thrombi in vessels, organising and sclerotic infarction all in the same case. This suggested, therefore, that an initial insult was followed by repeated thrombotic episodes, most likely due to the embolisation of tissue thromboplastin from the dead twin activating the extrinsic pathway of coagulation.[15 19]

The prognosis in the surviving monozygous twin livebirth is extremely poor. Of the 53 infants reported to date, 15 (28%) died and only 11 (29%) of the survivors were known to be neurodevelopmentally normal. In view of the deleterious effects of vascular disruption in the surviving twin we would recommend careful investigation after fetal death in utero in a twin pregnancy. If a dizygotic twin pregnancy cannot be excluded because a single placenta was seen on ultrasound and a monozygotic twin pregnancy is strongly suspected, delivery should be undertaken as soon as possible if the surviving cotwin is of sufficient maturity. When a surviving monozygous twin is delivered the infant should be monitored for seizures, abdominal masses, haematuria, or oliguria and should be investigated with ultrasound or radionuclide scans, or both, for evidence of cerebral, hepatic, splenic, and renal infarcts or necrosis.

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