SHORT REPORT

Autopsy after death due to extreme prematurity

D E Elder, J M Zuccollo

Arch Dis Child Fetal Neonatal Ed 2005;**90**:F270–F272. doi: 10.1136/adc.2004.062380

Autopsy reports for 29 very preterm infants dying at <28 days of age were reviewed. New findings were discovered in 79% and resulted in a significant change in diagnoses in 28%. Iatrogenic lesions were identified in 41% of cases and were the main cause of death in 14%.

When an extremely premature infant dies despite all intensive care efforts, it is accepted that the death certificate can be signed with the cause of death stated as ''extreme prematurity''. This fails to specify the exact reason for death, which may be due to various causes. Although new information is often obtained after neonatal autopsy, infants of lower gestation and birth weight are less likely to be autopsied.[1–5] This paper reports the utility of autopsy in our unit for infants born <28 weeks gestation and dying in the first 28 days of life.

METHODS AND RESULTS

A retrospective medical record audit was undertaken of all deaths of infants born <28 weeks gestation and cared for in the neonatal intensive care unit from January 1995 to December 2003. All autopsies were undertaken by a perinatal pathologist (JZ). The main cause of death was determined for all infants dying in the first 28 days of life.

Of 387 infants born less than 28 weeks gestation during the study period, 314 (87.2%) survived to discharge and one infant died at home soon after discharge. A total of 74 infants (29 female and 45 male) died during the study period. Of these, 54 infants died <28 days of age, and 29 (54%) of these were autopsied. Table 1 gives differences between those who did and did not have an autopsy. Infants who died <28 days of age and did not have an autopsy appeared to be slightly less mature and to have died sooner after birth. They were also less likely to be white.

For all but one of the 29 infants, the autopsy findings confirmed the specific reason for death. In one infant with sudden onset of pulmonary haemorrhage, the haemorrhage appeared to explain the failure to resuscitate but the reason for the pulmonary haemorrhage was not satisfactorily determined. In 23/29 (79%) cases, new diagnoses were discovered at autopsy. These are summarised in table 2 along with the final diagnosis.

The autopsy findings led to a significant change in the clinical diagnoses in 8/29 (28%) cases. In 12/29 (41%) cases, iatrogenic lesions were identified, and in four of these (14% of all 29 cases) the iatrogenic lesion was the main cause of death. Table 3 lists the iatrogenic lesions identified.

DISCUSSION

In this review, the autopsy added new information in nearly 80% of neonatal deaths for which extreme prematurity was thought to be the main cause of death. This resulted in a significant change in the main clinical diagnosis in 28% of cases.

Studies published over the last decade have shown low autopsy rates for preterm and very preterm infants.[2–5] Medical staff may not rate the autopsy as ''very important'' in cases of extreme prematurity.[2] Because we have shown the value of autopsy for those of our very preterm infants dying in the first month of life, we now consider it routine care to seek consent for autopsy for these infants.

We restricted analysis of autopsy data to those infants dying less than 28 days of age, as we felt that infants dying early were most likely to be assessed as dying solely because of their extreme prematurity. We found a significant change in the main clinical diagnoses in 28% of infants. One of the reasons for discord was the recognition at autopsy of iatrogenic lesions in 41%. These ranged from minor abnormalities to injuries that were considered sufficient to be the main cause of death. Other studies have found iatrogenic lesions at rates of 4.4–15%.[4 6 7] These rates may be lower than ours because of the inclusion of term infants. Awareness of iatrogenic lesions is important in auditing neonatal intensive care and can result in changes in policies and protocols. The extremely preterm infant appears to be particularly vulnerable to iatrogenic pathology, and in four of our cases this was the main cause of death.

We found that the autopsy information enabled us to be much more specific about the cause of death in these extremely premature infants. Some infants died because of complications of being born extremely preterm, such as lung disease of prematurity with air leak, whereas others died because of pregnancy and labour complications such as extreme growth retardation and perinatal asphyxia. The latter would probably previously have died in utero. An understanding of the true cause of death enables both the parents and the health professional caring for the baby to

Table 1 Basic data for infants dying after being born at <28 weeks gestation and admitted to the neonatal unit

	All infants who died (n = 74)	Infants who died ⩾28 days (n = 20)	Infants who died <28 days with PM (n = 29)	Infants who died <28 days without PM (n = 25)
Gestational age (weeks)	25 (21–27)	25 (23–27)	25 (22–27)	24 (21–27)
Birth weight (g)	675 (385–1236)	758 (445–1220)	680 (402–1236)	592 (385–1120)
Age at death (days)	6 (<1–406)	111 (29–406)	3 (<1–20)	1.42 (<1–17)
No (%) of white infants	48 (65%)	13 (65%)	23 (79%)	12 (48%)

Where applicable, values are median (range).
PM, Post mortem.

Table 2 New diagnoses found at autopsy in extremely preterm infants dying before 28 days of age

GA (weeks)	BW (g)	Age at death (days)	Main clinical diagnoses	New diagnoses at Autopsy	Significant change	Main cause of death
25	470	15	Lung disease with ongoing air leak. Asphyxial episode with pneumothorax. Presumed tracheal injury	Pulmonary haemorrhage. Pneumonia: right middle lobe. Cerebral cortical haemorrhage. Tracheal injury established	No	Iatrogenic: tracheal laceration
22	445	<1	Extreme prematurity. No active resuscitation. Twin	Meckel's diverticulum	No	Extreme prematurity: no active treatment
22	585	<1	Extreme prematurity. No active resuscitation. Twin of above infant	Evidence of perinatal asphyxia	Yes	Extreme prematurity with perinatal asphyxia: no active treatment
25	550	8	Bilateral cystic kidneys. Lung disease. Renal failure	Unilateral renal agenesis. Multicystic dysplastic kidney. Congenital pneumonia (renal ultrasound misinterpreted)	Yes	Congenital renal anomaly: absent kidney
27	880	8	Resolving lung disease. Collapse day 8	Long line perforation of right atrium with *S epidermidis* sepsis	Yes	Iatrogenic: long-line perforation
25	680	4	Fetal ventriculomegaly. Bilateral severe IVH. Hypovolaemic collapse	Congenital pneumonia. Multiorgan ischaemic changes	No	Perinatal infection
23	475	10	Resolving lung disease. Bilateral grade 3 IVH. ? NEC	Candida septicaemia with bowel perforation and cerebral abscess. Traumatic perforation of stomach	Yes	Postnatal Infection
26	670	5	Lung disease. Major pulmonary haemorrhage	Germinal matrix and subarachnoid haemorrhage. Periventricular leucomalacia	No	Pulmonary haemorrhage
24	650	<1	Clinical lung hypoplasia	Previous bowel perforation	No	Pulmonary hypoplasia
23	576	<1	Failure to resuscitate. Suspected pulmonary hypoplasia	Mild oligohydramnios sequence. Pulmonary aspiration of blood. Large retroplacental haemorrhage	Yes	Perinatal asphyxia
24	402	<1	Reverse Doppler flow. Cleft soft palate. Lung disease	Ventricular septal defect. Bilateral pleural effusions	No	Severe fetal growth restriction
27	810	<1	Clinical lung hypoplasia. Bilateral talipes. Oedema right leg	Hypoplastic R common iliac and R umbilical arteries	No	Pulmonary hypoplasia
27	880	2	Perinatal asphyxia. Right grade 4 IVH. Cerebellar haemorrhage	Right subdural haemorrhage. Global cerebral ischaemia. Ventricular septal defect	No	Perinatal asphyxia
27	830	8	Lung disease. Aortic thrombosis. Renal failure	Bilateral renal infarction. Bilateral adrenal necrosis. Pulmonary haemorrhage	No	Iatrogenic: aortic thrombosis with renal failure
23	420	2	Twin-twin transfusion. Donor twin. Lung disease. Pulmonary haemorrhage	Bilateral IVH grade 3. Haemorrhage around the right umbilical artery	No	Pulmonary haemorrhage
25	690	<1	Severe lung disease. Never stable after initial resuscitation	Aspiration of contaminated amniotic fluid. Severe placental disease	Yes	Severe respiratory disease due to antenatal aspiration of blood contaminated liquor
25	1012	19	Bilateral grade 3 IVH, PVL. Skin breakdown, right buttock. Pericardial & pleural effusions with TPN. Postnatal asphyxia	Fresh IVH and PVH haemorrhage. Focal adrenal necrosis. Pulmonary haemorrhage	No	Iatrogenic: long line perforation
25	700	19	Severe lung disease. *S aureus* septicaemia with shock and NEC	Pulmonary fibroplasia. Extensive myocardial necrosis. Oesophagus: multiple abrasions	No	Infection
24	692	8	Twin-twin transfusion. Recipient twin. Severe lung disease. Bilateral grade 4 IVH	Brain stem gliosis and PVL. Early NEC. Thrombus right umbilical artery	No	Severe HMD with PIE
25	994	13	Mild RDS. Haemorrhage ? pulmonary. *S epidermidis* cultured	Massive pulmonary haemorrhage	Yes	Pulmonary haemorrhage
25	414	20	Reversed Doppler flow. Severe lung disease. Small left kidney. Abdominal calcification	TPN hepatitis. Prenatal renal vascular thrombosis. Fresh cerebellar haemorrhage. Dystrophic calcification in bowel	No	Severe fetal growth restriction
27	1236	9	Abruption. Severe lung disease. Intestinal perforation. Bilateral IVH. Renal failure	Hypoxic-ischaemic injury in periventricular white matter. Gastric ulcerations. Oesophageal ulcerations. TPN effect with cholestasis	No	Perinatal asphyxia
24	680	<1	Deep decelerations. ? Supraglottic mass. Pneumothorax. Failure to resuscitate	Plug of mucoid material was found to occlude the tracheal lumen and extended the whole length of the trachea	Yes	Amniotic fluid plug in trachea after PPROM 1 week before delivery

GA, Gestational age; BW, birth weight; IVH, intraventricular haemorrhage; NEC, necrotising enterocolitis; PVH, periventricular haemorrhage; PVL, periventricular leucomalacia; HMD, hyaline membrane disease; PIE, pulmonary interstitial emphysema; TPN, total parenteral nutrition; PPROM, prolonged preterm rupture of membranes.

Table 3 Iatrogenic lesions found at autopsy in extremely preterm infants dying before 28 days of age

GA (weeks)	Age at death (days)	Iatrogenic lesion	Diagnosis made pre-mortem	Lesion cause of death?
25	15	Transection of trachea	Yes	Yes
25	8	Chorioamnionitis secondary to amnio-infusion congenital pneumonia	No	No
27	8	Cardiac tamponade due to long line	Uncertain	Yes
23	10	Perforation of stomach by orogastric tube	No	No
27	8	Aortic thrombus associated with umbilical catheter	Yes	Yes
23	2	Haemorrhage around the right umbilical artery associated with catheter insertion	No	No
25	19	Perforation of left subclavian vein with long line catheter	Yes	Yes
25	19	Oesophagus: multiple linear abrasions with haemorrhage	No	No
24	8	Thrombus right umbilical artery to above the aortic bifurcation	No	No
25	20	TPN related cholestasis	No	No
24	1	Injury to lung and heart secondary to needle aspiration of pneumothoraces	Heart known to have been punctured	No
27	9	Oesophageal ulceration. Gastric ulceration. TPN related cholestasis	No	No

TPN, Total parenteral nutrition.

realise that death was inevitable and may assist in prognostication for infants being cared for in the future. It is recognised that the chance of finding new information appears to be at least partly dependent on the quality of the autopsy and therefore the experience of the pathologist.[8] We are fortunate to have the services of an experienced perinatal pathologist, but most other tertiary and secondary perinatal units in New Zealand need to transport infants to Wellington for autopsy if they are to receive the same service.

This small study confirms the usefulness of autopsy when extreme prematurity is the main reason for death. This is especially so at the threshold of viability when it is important to understand why some of these very immature infants survive and why some do not. In our opinion the clinical experience gained in the past from autopsy on other extremely preterm infants helps the clinician to accept the inevitably of death when the outlook is extremely poor and be more confident when offering information and counsel to parents.

ACKNOWLEDGEMENTS

Thanks to Vaughan Richardson and Keith Fisher for assistance with access to the neonatal database.

Authors' affiliations

D E Elder, Department of Paediatrics, Wellington School of Medicine and Health Sciences, Otago University, Wellington, New Zealand

J M Zuccollo, Department of Obstetrics and Gynaecology, Wellington School of Medicine and Health Sciences, Otago University

Competing interests: none declared

Correspondence to: Dr Elder, Department of Paediatrics, WSMHS, PO Box 7343, Wellington, New Zealand; delder@wnmeds.ac.nz

Accepted 22 January 2005

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