Placental Pathology in Small for Gestational Age Infants

Abstract:
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Infants with intrauterine growth restriction (IUGR) and small for gestational age (SGA) have IUGR, and gross and microscopic examination is critical in explaining such cases. Reports of placentas from infants with a birth weight <2SD from the mean (approx 3rd centile) born between Jan 2004-Dec 2011 were evaluated. The principal pathology was determined in each case. Where two or more pathologic findings were present, they were ranked as principal and co-existing pathology in terms of severity of disease. Diagnosis and grading was as previously described 3. A small placenta was one weighing<350g (trimmed) at term. Data for acute pathologies e.g. acute chorioamnionitis were not included. The hospital operates a clinically oriented triage system that ensures that placentas of interest are examined. Included in these are cases less than or equal to the third centile, corrected for gender. At delivery, small sections of cord, membranes and parenchyma are sampled and stored and are available for subsequent histologic evaluation in the event of neonatal complications. Standard placental evaluation included gross examination and microscopic evaluation of two cross-sections of umbilical cord, two sections of membranes, and 5 sections of parenchyma taken from the inner two-thirds of the disc.

Introduction
Infants that are small for gestational age (SGA) not only have increased perinatal morbidity and mortality, but are also at risk of obesity, diabetes and heart disease in later life 9. Some of these infants may be growth restricted, and diabetes not all small for gestational age infants (SGA) have IUGR. Placental disease is an important cause of IUGR, but also pre-eclampsia, abruptio placentae, spontaneous abortion and preterm labour, a spectrum of other complications (referred to as “the great obstetric syndromes”) are due to shallow placenta is regarded as abnormal, and emphasises the relevance of placental examination in this cohort by specialised 11. We

Methods
Reports of placentas from infants with a birth weight <2 SD from the mean (approx. 3rd centile) born between Jan 2004-Dec 2011 were evaluated. Exclusion criteria were multiple gestation, known congenital anomaly, or gestational age <24 weeks. The cohort included a small number of stillborn who were stillborn. The principal pathology was determined in each case and assigned to a category 1-8 as given in the table below (Table 1). Where two or more pathologic findings were present, they were ranked as principal and co-existing pathology in terms of severity of disease. Diagnosis and grading was as previously described 3. A small placenta was one weighing<350g (trimmed) at term. Data for acute pathologies e.g. acute chorioamnionitis were not included. The hospital operates a clinically oriented triage system that ensures that placentas of interest are examined. Included in these are cases less than or equal to the third centile, corrected for gender. At delivery, small sections of cord, membranes and parenchyma are sampled and stored and are available for subsequent histologic evaluation in the event of neonatal complications. Standard placental evaluation included gross examination and microscopic evaluation of two cross-sections of umbilical cord, two sections of membranes, and 5 sections of parenchyma taken from the inner two-thirds of the disc.

Results
There were 69,493 deliveries over the study period. Four hundred and sixty one SGA cases were identified. On review, 21 were excluded as above. No placental histology was available in a further 44 cases, leaving a study group of 396 cases. Examination with full sampling, microscopic interpretation and diagnosis was available. A further 16 cases had placental tissue sampled in the delivery ward – while this allowed microscopic placental examination, it ensured that placentas of interest are examined. Included in these are cases less than or equal to the third centile, corrected for gender. At delivery, small sections of cord, membranes and parenchyma are sampled and stored and are available for subsequent histologic evaluation in the event of neonatal complications. Standard placental examination included gross examination and microscopic evaluation of two cross-sections of umbilical cord, two sections of membranes, and 5 sections of parenchyma taken from the inner two-thirds of the disc.

Discussion
This study reveals placental pathology in over 85% of cases of SGA infants (88% if a small but histologically normal placenta is regarded as abnormal), and emphasises the relevance of placental examination in this cohort by specialised pathologists working closely with obstetricians and neonatologists. Placental pathology was determined in each case and assigned to a category 1-8 as given in the table below (Table 1). Where two or more pathologic findings were present, they were ranked as principal and co-existing pathology in terms of severity of disease. Diagnosis and grading was as previously described 3. A small placenta was one weighing<350g (trimmed) at term. Data for acute pathologies e.g. acute chorioamnionitis were not included. The hospital operates a clinically oriented triage system that ensures that placentas of interest are examined. Included in these are cases less than or equal to the third centile, corrected for gender. At delivery, small sections of cord, membranes and parenchyma are sampled and stored and are available for subsequent histologic evaluation in the event of neonatal complications. Standard placental examination included gross examination and microscopic evaluation of two cross-sections of umbilical cord, two sections of membranes, and 5 sections of parenchyma taken from the inner two-thirds of the disc.

Villitis is a third trimester phenomenon that is found in approximately 11% of placentas 12. It is usually low-grade, with high-grade villitis found in less than 2% of placentas. High-grade villitis was over-represented in SGA infants in our series, being identified in almost 10%. Villitis is usually an immunologic phenomenon and may impact on fetal growth by decreasing placental reserve, but it is also associated with neurologic impairment 12,13. Some of these infants may be growth restricted, and it is associated with IUGR, but also pre-eclampsia, abruptio placentae, spontaneous abortion and preterm labour, a spectrum of other complications (referred to as “the great obstetric syndromes”) are due to shallow placenta is regarded as abnormal, and emphasises the relevance of placental examination in this cohort by specialised 11. We
in subsequent pregnancies. The latter two were uncommon in our study (20 cases, 5.1%), but are important clinical findings.

A major strength of this study was the availability of placental tissue in 90% of cases of interest. This is the result of a robust triage system with continuous active participation by delivery ward staff encouraged by obstetricians and neonatologists. In our institution, should any placenta not be submitted for pathological examination immediately after birth, a placental sample remains available for 1 year for retrospective microscopic examination. This allowed us to retrieve a further 16 cases, otherwise not available for microscopic interpretation. Limitations common to retrospective studies were the use of population norms rather than individualised values in assessing infants. Individualised assessment enables more rigorous separation of SGA from IUGR. While this was not a controlled study, the figures for prevalence of disease (Table 1) are from a large controlled study (816 cases) in an Irish population and, as we feel, valid for comparison with the current findings. Assessment of other variables such as cord coiling changed over the time period of this study and as such were not presented here. We feel that the use of the 3rd centile optimises the relevance of this study in focusing on a group at risk of increased morbidity and mortality. Examination of the placenta can provide valuable information to parents and clinicians in the majority of cases, and may include findings that impact on the management of subsequent pregnancies.

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