Placental Pathology in Small for Gestational Age Infants

Abstract:

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Abstract

Infants with intrauterine growth restriction (IUGR) are at an increased risk of perinatal disease, including death. Many, but not all small for gestational age infants (SGA) have IUGR. Placental disease is an important cause of 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 in terms of severity. There were 69,493 deliveries over the study period. 461 SGA cases were identified. No placenta was available in 44 cases, and 21 cases of known anomalies were excluded, leaving a study group of 396 cases. Pathology potentially causing or contributing to SGA and/or IUGR was identified in 84.1% of cases. Significant co-existing pathology was seen in 88 cases (22%). Placental examination provides key information in understanding abnormal fetal growth.

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[1]. Some of these infants may be growth restricted, and distinguishing between intrauterine growth restriction (IUGR) and SGA can be problematic[2]. IUGR and SGA are variably defined as less than the 10th, 5th or 3rd centiles: the use of the smaller centiles mean that constitutionally small normal infants are less likely to be included. Regardless of the presence or absence of growth restriction, morbidity and mortality are increased among infants born at term whose birth weights are at or below the 3rd centile[3]. Women who deliver an SGA infant in their first pregnancy are significantly more likely to deliver an SGA infant in their second pregnancy[4].

Placental disease is an important contributing factor to intrauterine growth restriction. Gross and microscopic examination of the placenta permits an assessment of some factors that affect intrauterine growth, and information gained may not just explain the current pregnancy outcome, but may also influence management of subsequent pregnancies[1]. The[5] value of placental examination has been emphasised by the Lancetâ s Stillbirths Series steering committee in 2011[5]. The increasing importance of standards in placental examination was emphasised by the publication for the first time of a dataset guiding placental examination in 2011 by the Royal College of Pathologists (UK)[6]. We report the findings in a cohort of placentas from SGA infants, which we defined as <3rd centile, from a single institution over an 8 year period and discuss the importance of the placental pathologies identified.

Methods

Reports of placentas of 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 babies 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[7,8,9,10]. 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[2]. At delivery, small sections of cord, membranes and parenchyma are sampled and stored and are available for subsequent histologic evaluation in the event of a neonatal complication. 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. In 380 of these, a complete macroscopic examination with full sampling, microscopic interpretation and diagnosis was available. A further 16 cases had placental tissue sampled in the delivery ward â while this allowed microscopic examination, a full gross examination on these cases was not available. Pathology potentially causing or contributing to SGA was identified in 84.1% of cases (Table 1). Uteroplacental insufficiency/ischaemia was the most common finding and was the primary pathology in 37.4% of cases.Co-existing pathology was found in 88 (22 %) of cases. The small number of cases in the â otherâ category (5, 1.3%) mostly showed chorangiosis, felt to be an adaptive response of the placenta rather than a cause of SGA

Discussion

This study reveals placental pathology in over 84% 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. IUGR/SGA may be regarded as the late manifestation of many different diseases with different causes[7]. Placental disease contributing to SGA can broadly be categorised as either maternal or fetoplacental in aetiology. Maternal factors include chronic disease, hypertension and vasculopathy. In addition to congenital and chromosomal anomalies, fetoplacental factors include abnormal placentation, immunologic reactions such as villitis, and thrombotic disease[8]. The understanding of these requires integration of macroscopic and microscopic findings with clinical outcome. Evidence of UPI was the most common pathologic finding in our review(37.4%) and is consistent with that of other workers[7]. Recent work suggests that UPI and a spectrum of other complications (referred to as â the great obstetric syndromesâ) are due to shallow implantation. Successful placentation requires remodelling of the spiral arterioles following implantation of the blastocyst. The size of the placental bed and the depth of the arteriolar transformation are two major factors determining sufficient maternal blood flow to the placenta, with deep placentation involving transformation of approximately 100 arterioles in the decidual and myometrial segments. Defective deep placentation is not only associated with IUGR, but also pre-eclampsia, abruptio placentae, spontaneous abortion and preterm labour, a spectrum of disorders characterised by uteroplacental insufficiency[9].

Villitis is a third trimester phenomenon that is found in approximately 11% of placentas[10]. 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[11]. Similarly, damage to the fetal microcirculation caused by fetal thrombotic vasculopathy (FTV) is associated with growth restriction and neonatal encephalopathy[8,10]. Delayed villous maturation (DVM), also called distal villous immaturity(DVI), was seen as the principal pathology in 15.2% of our cases. DVM/DVI is associated with maternal metabolic disease, diabetes, glucose intolerance and obesity. Its role in SGA remains to be clarified: some reports make an association with intrauterine fetal death and growth restriction[12], but a retrospective study carried out in our own institution showed IUGR was less common with DVM/DVI than with controls[13]. Microscopic placental examination revealed co-existing chronic pathology in 22% of our cases. In some cases, given the prevalence of disease, this maybe a chance association. However, we have previously shown that FTV is found four times more frequently than expected in cases of uteroplacental ischaemia[14]. The finding of two pathologies is therefore not surprising. Placental findings in SGA may not just explain the outcome of the index pregnancy, but may provide information that can assist in management of subsequent pregnancies. Villitis[15], increased perivillous fibrin and chronic histiocytic intervillositis may all recur

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[10] the figures for prevalence of disease (Table 1) are from a large controlled study (816 cases) in an Irish population[10] and are, we feel, valid for comparsion 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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Acknowledgements

Midwifery staff, National Maternity Hospital; Anatomic Pathology Technicians Mr P Dingle and Mr J Long.

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