Correlation of Placental Pathology with Perinatal Brain Injury

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KEYWORDS

• Perinatal brain injury • Placental pathology • Neurodisability

ABSTRACT

The purpose of placental pathology is to explain adverse clinical outcomes. One of the most tragic of these outcomes is perinatal brain injury with subsequent neurodisability. Findings in the placenta can play an important role in documenting sentinel events, uncovering clinically silent thromboinflammatory disease processes, revealing developmental alterations in functional reserve, and suggesting alterations in related maternal and fetal physiology. These findings, when integrated with clinical data, provide a plausible explanation for an otherwise unexpected outcome and can be helpful for treating physicians and family members.

OVERVIEW: PERINATAL BRAIN INJURY

Cerebral palsy (CP) and related forms of neurodisability related to perinatal brain injury occur in approximately 2 to 3 of 1000 live births.[1] Although the proportion of cases occurring in very low-birthweight (VLBW) infants is rising, a majority of cases (50%–60%) continue to involve term and near-term gestations delivering after 34 weeks. Overriding risk factors in the VLBW population include developmental immaturity, underlying fetal growth restriction (FGR), cardiopulmonary instability in early neonatal period, and infections occurring before and after birth. Placental pathology in VLBW infants, although important, plays a circumscribed role by determining causes of FGR and identifying significant fetal inflammatory responses (FIR) to infection. The causes of neurodisability in term and near-term infants are less clear and placental pathology can play a major role in identifying processes that contribute to central nervous system (CNS) injury.

To properly evaluate these placental processes, it is important to document a thorough gross examination and submit an adequate number of sections, sampling each placental compartment. Synoptic elements of an adequate gross examination are listed in **Box 1**. Particularly important are the trimmed weight of the placenta, the color of the fetal surface, and careful examination of the umbilical cord (UC) for length, extent of coiling, color, and type of insertion. Many placentas are adequately sampled with 3 tissue blocks, but cases of gross abnormalities or a clear clinical history of adverse outcome usually require additional sections. At minimum, 2 cross-sections of UC, 1 membrane roll that includes a piece of the attached marginal placental parenchyma, and 2 full-thickness sections taken within the inner two-thirds of the parenchyma are needed. The chorionic plate is more critical than the basal plate, but both should be sampled. One of the parenchymal sections is ideally taken at the UC insertion site.

Systematic evaluation of a specific set of histologic parameters in every placenta is the key to not missing important diagnoses (**Table 1**). Maternal vascular processes are identified by assessing placental weight, fetoplacental weight ratio, UC diameter, altered maternal arterioles in the membrane roll, developmental abnormalities in the basal plate, and villous changes related to partial or complete obstruction of maternal blood flow in the placental parenchyma. Fetal vascular processes are assessed by evaluating the diameter, muscular wall, and luminal patency of large fetal

The author has nothing to disclose.
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Surgical Pathology 6 (2013) 153–180
http://dx.doi.org/10.1016/j.path.2012.11.005
1875-9181/13/$ – see front matter

Box 1
Synoptic elements in the gross description

- Trimmed placental weight
- Color of fetal surface and UC
- Assessment of fragmentation and completeness of basal plate
- Length and site of UC insertion (in centimeters from the placental margin)
- Documentation and description of firm, hemorrhagic, and cystic lesions

vessels in the UC, chorionic plate, and major stem villi and by recognizing karyorrhexis or absence of capillaries in the dependent distal villous tree. The diagnosis of inflammatory processes involves assessment of the membranes, subchorionic fibrin, and distal villi. Finally, an increase in circulating nucleated red blood cells (NRBCs) should be excluded in all term or near-term placentas.

Table 1
Checklist for histologic evaluation

UC sections	FIR Decreased fetal extracellular fluid (Wharton jelly)
Membrane rolls	Meconium changes Chorio(amnio)nitis Decidual arteriopathy
Chorionic and large stem villous vessels	Inflammation, thrombosis, necrosis, luminal dilatation
Chorionic plate	Pigment-laden macrophages Cellular infiltrates in chorion/subchorionic fibrin
Margin and basal plate	Retroplacental hemorrhages, plasma cells, accreta
Villi, low-power magnification (2×–4×)	Overall maturation (immature/slightly immature/mature) Regional variations in architecture Localized changes in character Foci of agglutination
Villi, higher-power examination (10×–40×)	Definitive diagnosis of villous alterations Assessment of circulating fetal NRBCs

SENTINEL EVENTS/TOTAL ASPHYXIA

OVERVIEW

Total asphyxia is an important cause of CNS injury, and severe placental perfusion defects resulting in asphyxia are often referred to as *sentinel events*.[2,3] The obstetric syndrome associated with a sentinel event is called *birth asphyxia* and has a specific definition that includes low cord pH and/or elevated base excess. The corresponding depressed neurologic state in a newborn is known as hypoxic-ischemic or, more properly, neonatal, encephalopathy (NE). Although both clinical and experimental studies suggest that a majority of infants born after total asphyxia either die or recover without sequelae, a minority of survivors develop CP, usually of the spastic quadriplegic type with severe associated developmental disabilities.[4] A considerable amount of attention has been paid over the past 20 years to separating cases of pure birth asphyxia from cases of more complex causation. The current consensus is that approximately 15% of CP in term and near-term infants is due to pure birth asphyxia and that 20% of infants presenting with NE have an isolated preceding sentinel event.[5] The remaining cases are of mixed cause and often associated with significant placental pathology. Another consideration in all cases of suspected sentinel events is to exclude conditions that mimic birth asphyxia, such as birth trauma, Rett syndrome, molybdenum cofactor deficiency, and mitochondrial disease.

The 4 major clinical categories of sentinel events are

1. Premature separation of the placenta from the uterus due to abruptio placenta or uterine rupture
2. Obstruction of fetoplacental blood flow due to UC occlusion
3. Fetal hemorrhage
4. Maternal hypotension

The last category is not usually associated with placental findings and is not discussed further.

ABRUPTIO PLACENTA/UTERINE RUPTURE

Abruptio placenta (acute abruption) is caused by rupture of 1 or more of the maternal spiral arteries that supply the placenta. Risk factors include preeclampsia, vasoactive drugs (cocaine and nicotine), and sheer forces associated with trauma or heavy physical labor. Uterine rupture usually occurs in uteri weakened by a previous cesarean section scar. Both result in large retroplacental