

Section I

Techniques and Practical Considerations: Approach to Autopsy of the Perinatal Nervous System

Chapter

Clinical Considerations

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The initial steps in the process of perinatal nervous system evaluation, namely the planning of the optimal approach and choice of samples to be obtained, are driven by the clinical context. Of key importance are the following data:

- a. Gestational age at the time of demise (if stillborn) or gestational age and postnatal age (if liveborn), for comparison with normative standards of development (see the Appendix)
- b. State of maternal health (age, parity, preexisting medical conditions or ones appearing during gestation or around the time of delivery, exposure to medications/toxins/infections) and health of siblings or other family members
 - Concerns for inherited (i.e., genetic) conditions, metabolic disorders, congenital infections, and so forth, may indicate the need for special testing.
- c. Details of prenatal course, including any imaging, amniocentesis, or monitoring
 - Prenatal imaging modalities most commonly consist of transabdominal ultrasonography, typically done at the time of the first prenatal visit (to confirm pregnancy) or more typically in the mid–second trimester for the detection of fetal or placental anomalies. If further detailed imaging is needed, maternal/fetal magnetic resonance imaging (MRI) may be undertaken (see Chapter 2).
 - Amniocentesis, with or without chorionic villus sampling (CVS), may be offered in specific circumstances (maternal age >35; abnormal maternal serum screening for alpha-fetoprotein [AFP], human chorionic gonadotropin [hCG], estriol [“triple screen”], and sometimes inhibin-A [“quadruple screen”]; prior history of fetal loss or abnormality; suspicion of anomalies on ultrasound), and karyotypes or more advanced genetic analyses (see Chapter 6) may be performed to aid the parents and practitioners in planning or decision-making.
 - Biophysical profiling (BPP) of the fetus in utero may be performed in high-risk cases (prior pregnancy loss, maternal vascular or other disease, twin or multiple pregnancy, abnormal amniotic fluid volume, Rh factor incompatibility, maternal report of decreased fetal movements). BPP includes electronic fetal heart rate monitoring, as well as an examination of breathing,

movements, muscle tone, and volume of amniotic fluid, usually in the last trimester. Each factor is assigned a value, summing to a score, which the practitioner may use to advise regarding whether to proceed with initiating delivery. This information assists in determining the nature of the likely causes of fetal demise and may help focus the overall autopsy.

- d. Details of labor and delivery, including intrapartum fetal monitoring data
- e. Findings in the placenta, even if only available as macroscopic observations from the delivering obstetrician or midwife (as discussed in more detail later in this chapter)

Depending on these data points, the prosector may choose to set aside tissue samples for confirmatory or ancillary support of otherwise standard autopsy examination (see Chapters 5–8).

Correlation with Placental Pathology and Prematurity

The placenta is best considered a vital organ of the fetus, as essential as the heart or lungs. In addition, it serves as the “diary” of the pregnancy, often indicating antepartum (maternal and exogenous) influences. It should be examined as a matter of routine in every stillbirth or adverse neonatal outcome for clues to underlying contributing factors.

The placental pathology of greatest importance to the vulnerable developing brain includes *vascular disease* (*maternal vascular underperfusion [MVUP]*) and *infection*. MVUP comprises the following placental pathologic features: those involving the villi and intervillous space (increased syncytial knots, villous agglutination, intervillous fibrin deposition, and distal villous hypoplasia), and those affecting the maternal vessels and implantation site (acute atherosclerosis, mural hypertrophy of membrane arterioles, muscularized basal plate arteries, increased giant cells at placental site, and immature intermediate trophoblast) [1]. Macroscopic factors such as low placental weight, large volume of infarcts, and thin umbilical cord should be taken into account, along with clinical features of pre-eclampsia. Thus, generally speaking, MVUP represents a threat to normal fetal growth, which, if severe, has a high likelihood of affecting the brain adversely, delaying development and/or resulting in lesions of hypoxia-ischemia. Recently, maternal plasma angiogenic index-1 (ratio of

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placental growth factor/soluble vascular endothelial growth factor receptor-1) has been identified as a potential clinical indicator of maternovascular (uteroplacental) underperfusion during pregnancy [2].

The role of ascending infection (typically heralded by premature rupture of membranes, maternal fever, and/or positive amniotic fluid cultures) in perinatal brain injury is based on an epidemiological relationship between placental abnormalities and subsequent neurodevelopmental abnormalities, often called “cerebral palsy” [3]. Depending on the study, various placental pathologic findings are linked to later neurodisability: fetal thrombotic vasculopathy, chronic villitis with obliterative fetal vasculopathy, chorioamnionitis with severe fetal vasculitis, meconium-associated fetal vascular necrosis [4], recent nonocclusive thrombi of chorionic plate vessels, and severe villous edema [5]. In general, the presence of more than one placental lesion increases the risk of neurological deficits.

Furthermore, specific placental lesions linked with brain injury may fall into the following categories of timing [6]:

- Acute (occurring within 0–6 hours of delivery): Maternal hypotension, abruptio placentae, complete total umbilical cord obstruction, and fetal vascular rupture

- Subacute (6 hours to 7 days before delivery): Cord entanglements, meconium-associated vascular necrosis, and fetomaternal hemorrhage
- Chronic (greater than 1 week before birth): Maternal vascular underperfusion, villous infarcts, villitis of unknown etiology, chronic abruption, and fetal thrombotic vasculopathy

Thus information from delivery records and placental pathology reports may provide clues regarding autopsy neuropathology.

Regardless of etiology, preterm delivery itself carries an elevated risk of brain injury, highlighted in greater detail in Chapters 29–36. For example, infants with very low birth weight (i.e., preterm infants) have elevated incidence of intraventricular hemorrhage in the setting of amniotic sac inflammation (chorioamnionitis, umbilical vasculitis, and amnion epithelial necrosis) compared to those without inflammation [7].

The neuropathologic substrate of cerebral palsy, whether related to MVUP or ascending infection, is essentially hypoxic-ischemic (see Chapters 29–36) [8].

References

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