OBSTETRICS

Classification of placental lesions

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Placental pathology can be useful in a variety of ways including immediate diagnosis of important conditions affecting the mother or infant, identifying conditions that are likely to recur in subsequent pregnancies, separating clinical syndromes into distinct pathological phenotypes for further investigation, and uncovering the underlying cause of unexpected adverse outcomes. Classification of placental lesions has evolved from being a purely descriptive exercise through a stage in which the major pathophysiological processes such as disorders of maternal implantation and the amniotic fluid infection syndrome were first described to a recently proposed comprehensive classification system that includes all of the major maternal and fetal vascular and infectious and idiopathic/immune inflammatory processes (Amsterdam Placental Workshop Group). Implementation of this unified system with reproducible grading and staging should help establish evidence-based recommendations for placental submission and facilitate progress in studying the pathogenesis, diagnosis, and treatment of obstetric disorders with an underlying placental etiology.

Key words: abruption, adverse pregnancy outcome, chorioamnionitis, clinical implications, delayed villous maturation, fetal vascular, maternal vascular, placenta, placental pathology, recurrent lesion, underperfusion, vascular lesions of the placenta, villitis

The placenta is the perennial Holy Grail, a putative diary of intrauterine life promising to explain the mysteries underlying poor pregnancy outcome. Its practical counterpart, placental pathology, is finally emerging as a respectable specialty after many years of confusion related to experts with divergent views, pathologists with varying levels of interest and relevant training, and nomenclature having little relationship to either the underlying biology or clinical presentation.

Recent progress has been realized through the gradual acceptance of a standardized, reproducible, and biologically based classification system. Much work remains to disseminate this new information to practicing pathologists and clinicians.

In this review, I will summarize the utility of placental diagnoses, review early contributions to our understanding of placental pathology, go into more depth describing the new Amsterdam international consensus criteria for placental diagnosis (Table 1), and conclude by speculating on how further progress in this area could facilitate the goals of the Human Placental Project to develop biomarkers and imaging techniques that can identify placental disease processes in real time when targeted intervention may be of benefit.[1,2]

Utility of placental examination

Submission of placentas for examination generally follows 1997 College of American Pathologists guidelines.[3] Approximately 40-50% of all placentas delivered in a high-risk setting will be examined according to these criteria.[4,5]

Additional high-quality evidence is needed to decide whether these guidelines are optimal for patient care. Useful information from a competently performed placental evaluation falls into the following 4 categories: (1) identification of previously unsuspected disease processes in the mother or infant that require immediate attention (eg, fragmentation suggestive of retained placenta or placenta accreta, unusual infections such as cytomegalovirus or listeria, and findings suggestive of aneuploidy or metabolic storage diseases); (2) conditions associated with a high probability of recurrence in subsequent pregnancies (Table 2); (3) information that can guide the management of future pregnancies or influence the long-term care of mother and infant (Table 3); and (4) diagnoses that provide a specific explanation for an adverse outcome such as fetal death, fetal growth restriction (FGR), spontaneous preterm birth, or central nervous system (CNS) injury.

These outcomes all have a wide differential diagnosis that placental pathology can sort through for the purposes of quality assurance, risk management, and patient education (Table 4). Although these benefits are important, a more thorough understanding of placental abnormalities could both expand and focus the utility of placental examination.

Background

Placental pathology in its earliest stages focused on macroscopic abnormalities such as battledore placentas, succenturiate lobes, and velamentous insertions of the umbilical cord (UC). Although distinctive, these conditions proved not to be closely related to adverse outcomes. A series of seminal studies published between 1970 and 1995 laid the groundwork for our present understanding of placental pathology. Pijnenborg et al[6] established the conceptual framework for disorders of placental implantation and their sequelae. Blanc[7] first delineated the sequence of placental changes that characterize amniotic fluid infection. Harris[8] distinguished marginal venous abruption

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Received May 4, 2015; revised May 15, 2015; accepted May 26, 2015.

The author reports no conflict of interest.

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0002-9378/$36.00

http://dx.doi.org/10.1016/j.ajog.2015.05.056

TABLE 1
Placental classification (incorporating the 2014 Amsterdam Placental Workshop Group criteria)

1. Placental vascular processes
   a. Maternal stromal-vascular lesions
      - Developmental
        - Superficial implantation/decidual arteriopathy
        - Increased immature extravillous trophoblast
      - Malperfusion
        - Global/partial
          - Early: distal villous hypoplasia
          - Late: accelerated villous maturation
        - Segmental/complete
          - Villous infarct(s)
      - Loss of integrity
        - Abruptio placenta (arterial)
        - Marginal abruption (venous)
          - Acute
          - Chronic
   b. Fetal stromal-vascular lesions
      - Developmental
        - Villous capillary lesions
        - Delayed villous maturation (maturation defect)
        - Dysmorphic villi
      - Malperfusion
        - Global/partial
          - Obstructive lesions of umbilical cord
          - Recent intramural fibrin in large fetoplacental vessels
          - Small foci of avascular or karyorhectic villi
        - Segmental/complete
          - Chorionic plate or stem villous thrombi
          - Large foci of avascular or karyorhectic villi
      - Loss of integrity
        - Large vessel rupture (fetal hemorrhage)
        - Small vessel rupture (fetomaternal hemorrhage)
        - Villous edema
2. Placental inflammatory-immune processes
   a. Infectious inflammatory lesions
      - Acute
        - Maternal inflammatory response: chorioamnionitis, subchorionitis
        - Fetal inflammatory response: chorionic/umbilical vasculitis
      - Chronic
        - Villitis (CMV, others)
        - Intervillositis (malaria, others)
   b. Immune/idiopathic inflammatory lesions
      - Villitis of unknown etiology and related/associated lesions
        - Chronic villitis
        - Chronic chorioamnionitis
        - Lymphoplasmacytic deciduitis
        - Eosinophil T-cell fetal vasculitis
      - Chronic histiocytic intervillositis
3. Other placental processes
   - Massive perivillous fibrin(oid) deposition (maternal floor infarction)
   - Abnormal placental shape or umbilical insertion site
   - Morbidly adherent placentas (accreta)
   - Meconium-associated changes
   - Increased circulating nucleated red blood cells

CMV, cytomegalovirus.

Redline. Classification of placental lesions. Am J Obstet Gynecol 2015.

from the much less common syndrome of arterial rupture and abruptio placenta. Benirschke and colleagues[9,10] described how early marginal venous abruptions could progress to the chronic abruption-oligohydramnios sequence and was the first to describe the important lesion known as maternal floor infarction. Stallmach et al[11] demonstrated the association between delayed villous maturation (maturation defect) and fetal death. Altshuler and Russell[12] brought idiopathic chronic villitis to attention, and Altshuler[13] was the first to describe villous chorangiosis. Finally, Sander[14] described the patterns that would later come to be known as fetal thrombotic vasculopathy (now segmental fetal vascular malperfusion).

A more systematic approach to placental diagnosis was undertaken by the Perinatal Section of the Society of Pediatric Pathology beginning in 1998.[15-17] Ensuing publications proposed and validated the grading and staging of lesions related to amniotic fluid infection and the maternal and fetal vascular disorders. Building on this work, a schematic framework for all placental lesions was presented at the International Federation of Placenta Associations meeting in 2006.[18] These efforts provided the background for a comprehensive system proposed by 26 placental pathologists from around the world who met in Amsterdam in September 2014.[1] The consensus recommendations agreed upon during this meeting and in subsequent online discussions are incorporated into the next section and have been submitted for publication.

A secondary goal of the meeting was to establish sampling guidelines for placental evaluation. Although not the focus of this review, the following recommendations were made: submit 4 blocks as a minimum; one to include 2 cross-sections of the UC and a roll of the extraplacental membranes including part of the marginal parenchyma; 3 others containing full-thickness sections of normal-appearing placenta parenchyma taken from within the central two thirds of the disc including one adjacent to the UC insertion site.

The proposed new framework for placental classification (Table 1) is discussed in the following text.

Placental vascular processes

The placenta is essentially an interhemal membrane mediating the exchange of