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PLACENTA
Placenta 28, Supplement A, Trophoblast Research, Vol. 21 (2007) S14–S22

In Utero Imaging of the Placenta: Importance for Diseases of Pregnancy

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Accepted 9 February 2007

Abstract

Maurice Panigel demonstrated by X-rays, almost 40 years ago, placental maternal blood jets in non-human primates. Although to researchers the importance of the placenta is evident, in clinical obstetrical imaging, the fetus takes precedence. The placenta is imaged almost as an after thought and mostly to determine its location in the uterus. In animal species, the placenta was imaged with techniques which would be considered too invasive (or too costly for routine use) in humans, many pioneered by Panigel: radioangiography, radioisotopes scintigraphy, thermography, magnetic resonance imaging (MRI) and spectroscopy, positive emission tomography (PET) and single photon emission computed tomography (SPECT). Ultrasound allows for detailed, and, as far as is known, safe analyses of not only placental structure in the human but also its function. Earlier, only 2-dimensional grey-scale was available and more than 20 years ago, placental grading was popular. Later, colour imaging and spectral Doppler analysis of blood velocity both in the umbilical artery and within the placenta as well as the uterus and fetal vessels became essential and, more recently, the use of ultrasound contrast agents has been described, albeit not yet in a clinical setting. Three-dimensional ultrasound permits evaluation of the placenta in several planes, more precise depiction of internal vasculature as well as more accurate volume assessment. Several medical disorders of the pregnant woman or her fetus begin or end in the placenta, and ultrasound is the optimal investigation method. Obvious examples include pre-eclampsia and other forms of hypertension in pregnancy, less than optimal fetal growth (i.e. intrauterine growth restriction), triploidy (and its placental manifestation: partial mole), non-immune hydrops as well as several infectious processes. Ultrasound is also particularly suited to evaluate specific placental conditions, such as abnormal placentation (placenta previa and accreta for instance), gestational trophoblastic disease and placental tumors (e.g. chorioangioma).

Keywords: Placenta; Ultrasound; Pregnancy; Fetal–maternal circulation; Pre-eclampsia

1. Introduction

The notion of placental circulation dates from Antiquity. At the end of the first century AD, Soranus of Ephesus, in his ''Treaty of women illnesses'', described the chorion, amnion and the cord, containing 4 vessels and a urinary channel [1]. At the time and for many years to come, approximately the middle of the 16th century in fact [2], maternal and fetal circulations were thought to be continuous. Over the ensuing years, arguments continued regarding the purely fetal versus shared origin of the placenta and the timing of the connection between the two systems (see historical perspectives [3,4]). The question of exactly when is the actual uteroplacental circulation established, posed by Ramsey and Donner [5] is still debated [6,7].

Many imaging techniques have been used in the last 50 years [8], culminating in ultrasound and all its modalities: starting with regular B-mode [9], spectral [10,11], power, also known as energy or colour angio [12] and colour Doppler [13], 3D/4D [14,15] and, more recently, ultrasound contrast agents [16]. These have allowed *in situ* observation of the

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0143-4004/$ - see front matter © 2007 Published by IFPA and Elsevier Ltd.
doi:10.1016/j.placenta.2007.02.004

placenta and have elucidated in part some of the long-standing questions on the aetiology of several gestational conditions, such as pre-eclampsia and intrauterine growth restriction (IUGR). In this review, some facts on placental implantation will be detailed as well as past, present and future imaging modalities and their importance in diagnosing or predicting pregnancy complications. Some of these complications will be discussed, more from the imaging standpoint that in detailed clinical aspects.

2. Placental development

While a detailed analysis of maternal–fetal communications is well beyond the scope of this article, some details may be helpful in understanding the aetiology of certain pregnancy conditions, their manifestations in the placenta and the contribution of imaging techniques in interpreting changes occurring as a result of these situations. Anomalies on the maternal side, rather than the fetal side are, generally, at the origin of later pathological conditions. The interested reader is referred to a recently published excellent discussion of implantation, trophoblastic invasion and remodelling changes occurring in the uterine spiral arteries [17].

Invasion of the myometrium (maternal tissue) by the trophoblast (fetal origin) has traditionally been described as occurring in two phases: first (up to 12 weeks) and early second (12–16 weeks) trimesters [18]. More recently, this process has been depicted as progressive rather than biphasic [19], although there does not seem to be absolute certainty regarding one or the other [17]. This trophoblastic invasion transforms the normally coiled uterine spiral arteries into open and straight vessels, causing resistance to fall dramatically in the uterine arteries, as can be demonstrated with spectral Doppler [20]. Abnormal placentation may allow either lower levels of O_2 with resulting villous hypervascularisation, as seen in pre-eclampsia or higher than normal levels with abnormal branching and fetal growth restriction [21,22]. If, on the contrary, the capillary obliteration is incomplete, excessive entry of maternal blood at a very early stage inside the developing placenta results in oxidative stress and subsequent degeneration of villous tissue [23]. Documentation of blood flow in the intervillous space in cases of first-trimester miscarriage by colour Doppler is useful in the prediction of success or failure of expectant management [24]. Premature and diffuse onset of intervillous blood flow can be detected by grey-scale and colour imaging and confirmed by spectral Doppler. This abnormal blood flow pattern may increase the oxidative stress on the early placental tissue, subsequently impair placental development and is often associated with early pregnancy failure [25]. The continuing invasion (referred to by some as the second invasion phase) may occur as late as 20–24 weeks. Spiral arteries are widely open, resulting in a further drop in the impedance in the uterine arteries and a major increase in the end-diastolic velocity, as documented by Doppler velocimetry [20]. Both syncytiotrophoblast and cytotrophoblast growth, development and invasion are regulated by an apoptosis cascade within the villous trophoblast [26]. This cascade is active in the earlier stages of trophoblastic invasion and becomes reactivated several weeks later. Derangement in the cascade (upregulation) and abnormal secondary invasion is thought by most to be the phenomenon at the origin of pre-eclampsia. If severe, it can also be responsible for early miscarriages while, if less severe, it may induce other pathological conditions, such as IUGR [19,26]. Extravillous trophoblast apoptosis, however, has been found to be reduced in pre-eclampsia [27]. In 75–90% of cases of ''placenta-induced'' IUGR, uterine artery will demonstrate abnormal Doppler velocimetry [24,27]. Endothelial dysfunction too is involved in the process of abnormal placentation in pre-eclampsia and IUGR [26,29]. Abnormal uterine artery Doppler velocimetry is observed in most cases of early onset pre-eclampsia and IUGR, in association with laboratory signs of endothelial dysfunction and less in late-onset pre-eclampsia where such dysfunction is not observed [28].

3. Imaging technologies

There is a large variety of techniques for placental imaging, many of them pioneered by Panigel in animal imaging, such as radioisotope scintigraphy, thermography and magnetic resonance imaging with gadolinium [8]. Some early technologies were used in animals with variable degrees of success but less in humans, in some cases because of concerns for safety of the fetus. Presently ultrasound and, to a much lesser extent, magnetic resonance imaging, are the options of choice for imaging of the placenta in health and disease. In the future, the use of ultrasound contrast agents will, undoubtedly, bring further understanding to placental implantation process and physiopathology.

3.1. Early technologies (for more details and references, see [8])

These have been used successfully as a placental imaging technique but mostly in animal and laboratory setups because they are far too invasive for human studies: conventional X-rays, particularly angiography, with injection of contrast agents; computer-assisted tomography; radionuclide scintigraphy to localise implantation, study haemodynamics and diagnose placenta previa; thermography; magnetic resonance imaging and its variations, such as microscopic MR, MR angiography, particularly with gadolinium DTPA, MR spectroscopy; and positron emission tomography (PET) which allows analysis of materno-fetal transport and placental blood volume. Some, if not most of these methods (except MR) are contraindicated in the pregnant human and have essentially been replaced by ultrasound.

3.2. Where are we now?

3.2.1. Ultrasound

Ian Donald is credited with the first publication, in 1958, in the Lancet, on the use of ultrasound in abdominal masses, Since then, its use has burgeoned to a point that virtually every pregnant woman who receives prenatal care will have, at least, 1