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Redness discordance in monochorionic twin placentas: Correlation with clinical and placental findings

Monique E. De Paepe [a, b, *], Füsun Gündoğan [a, b], Quanfu Mao [a], Sharon Chu [a], Svetlana Shapiro [a]

[a] Department of Pathology, Women and Infants Hospital, Providence, RI, 02905, United States
[b] Department of Pathology and Laboratory Medicine, Alpert Medical School of Brown University, Providence, RI, 02905, United States

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ABSTRACT

Introduction/Objectives: Recent studies suggest redness (color) discordance of the placental basal plate may be a marker for twin anemia-polycythemia sequence (TAPS), a recently described complication of diamniotic-monochorionic twinning characterized by marked intertwin hemoglobin (Hb) discordance in the absence of oligohydramnios-polyhydramnios. In this study, we determined the clinicoplacental and choriovascular correlates of basal plate color discordance in monochorionic twin placentas, and assessed its value as postnatal indicator of TAPS.

Methods: We performed a clinicoplacental analysis of 100 consecutive non-TTTS diamniotic-monochorionic twin placentas with available photographic documentation of the basal plate. Basal plate redness was quantified by computer-assisted analysis of digital images and expressed as intertwin color difference ratio (CDR).

Results: The CDR ranged between 1.00 and 3.58 (median CDR: 1.14; 90th %ile: 1.98). Compared to twins with low CDR (N = 90), twins with high CDR (≥2.0; N = 10) had significantly higher hemoglobin difference (11.25 g/dL versus 2.55 g/dL) and significantly fewer and smaller artery-to-artery (AA) and artery-to-vein (AV) anastomoses. Apgar scores and birth weights were equivalent in both groups. Among the 10 twin sets with high CDR, six (60%) qualified as TAPS, as defined by intertwin Hb difference >8 g/dL and absent or very small AA and AV anastomoses. Conversely, 6 of 8 (75%) twin sets with TAPS had a CDR ≥ 2.0.

CONCLUSION: Intertwin CDR correlates with intertwin hemoglobin difference and chorionic angioarchitecture. A CDR value ≥ 2.0 (the 90%ile value for CDR derived from the present cohort) has high specificity (96%), but relatively low positive predictive value (60%) as indicator of TAPS, as currently defined.

1. Introduction

Monochorionic twins (20–25% of all twins) share a single placenta and are virtually always connected through intertwin choriovascular anastomoses [1–3]. These anatomic characteristics form the basis of unique complications of monochorionic twinning, such as severe chronic twin-to-twin transfusion syndrome (TTTS)/twin oligohydramnios-polyhydramnios sequence (TOPS), twin reversed arterial perfusion (TRAP) sequence, and acute peripartum twin-to-twin transfusion.

Each of these complications has been associated with more or less typical – albeit not pathognomonic – placental and choriovascular characteristics [4–8]. Based on these prevalent placental associations, examination of the monochorionic twin placenta traditionally has focused on the appearance of the fetal surface. The recent description of twin anemia-polycythemia sequence (TAPS) as a distinct complication of monochorionicity may have resulted in increased emphasis on the appearance of the maternal surface (basal plate) of the placenta, as well. TAPS is a form of chronic and slow intertwin blood transfusion that results in large intertwin hemoglobin differences without associated (severe) twin oligohydramnios-polyhydramnios sequence [9,10]. The pathogenesis of TAPS has been linked to its typical placental

* Corresponding author. Women and Infants Hospital, Dept. of Pathology, 101 Dudley Street, Providence, RI 02905, United States.
E-mail address: mdepaepe@wihri.org (M.E. De Paepe).

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angioarchitecture, characterized by the presence of only few and small intertwin anastomoses [4,11,12]. TAPS may occur spontaneously (estimated incidence: 3–6% of monochorionic twin pregnancies, typically after 26 weeks' gestation) or iatrogenically following laser treatment for TTTS (estimated incidence: up to 16% of laser-treated TTTS pregnancies, typically 1–5 weeks after surgery) [4].

TAPS may be diagnosed antenatally [13]. In about half the cases, TAPS is only identified postnatally [14,15], when it is suspected in the presence of a large intertwin hemoglobin difference (>8 g/dL) at birth [16]. Two additional criteria have been proposed to distinguish TAPS from acute peripartum twin-to-twin transfusion: high reticulocyte count in the donor (intertwin reticulocyte ratio >1.7) (as evidence of chronic anemia) [16] and/or the presence of small (<1 mm) (residual) intertwin anastomoses, usually detected by vascular injection [4].

Reticulocyte counts and vascular injection studies are not always available to support a TAPS diagnosis. Therefore, the presence of a distinct color difference between the two placental shares, observed from the maternal side of the placenta, has been proposed as additional postnatal TAPS criterion (pale parenchyma on the side of the anemic twin and dark red parenchyma on the side of the polycythemic twin) [17–19]. In a recent study, Tollenaar et al. [19] described a technique for quantitation of intertwin color (redness) discordance in twin placentas, based on computerized analysis of digital images, and coined the term 'color difference ratio' (CDR) as quantitative measure of intertwin basal plate color discordance. In their series, all TAPS placentas (N = 19) had a CDR value > 1.5, whereas none of the placentas from the uncomplicated monochorionic twin placentas control group had a CDR > 1.5. This suggested a CDR value > 1.5 may be a reliable (possibly pathognomonic) indicator of TAPS.

The aims of the present study were 1) to establish reference values for intertwin redness concordance/disparity in a large cohort of monochorionic twin placentas; 2) to determine the clinical and placental correlates of intertwin placental color discordance; and 3) to determine the value of intertwin placental color discordance as postnatal marker of (spontaneous) TAPS, as defined by a Hb difference of > 8 g/dL in the presence of tiny placental anastomoses.

2. Methods

2.1. Patient population

We performed a retrospective analysis of a cohort of diamniotic-monochorionic twin placentas examined at the Department of Pathology at Women and Infants Hospital between 2010 and 2016. The following exclusion criteria were applied: remote (>48 h prior to delivery) fetal demise of one or both twins, pregnancies complicated by TTTS, delivery prior to 23 weeks' gestation, higher order multiple (>2 fetuses) gestation, monoamniotic placentas, placentas without photographic documentation of the basal plate, placentas in which vascular injection could not be performed due to disruption of the chorionic plate, and placentas with large amounts of adherent blood clot, precluding reliable image analysis of color intensity of the basal plate.

The accompanying charts of the eligible cases were reviewed for relevant maternal and fetal/neonatal information, such as gestational age, pregnancy complications, presence of intrauterine growth restriction (<10th percentile for age), presence/absence of TTTS, and presence/absence of congenital/chromosomal anomalies. The presence or absence of TTTS, defined by the sonographic determination of twin oligohydramnios/polyhydramnios sequence (TOPS) in a monochorionic gestation, was based on well-established criteria [20]. The neonatal charts were reviewed for relevant information, including birth weights, Apgar scores, gender, and first hematologic blood count values (hemoglobin and hematocrit, obtained immediately after delivery). Following review of the placental characteristics, twin pregnancies were classified as TAPS or non-TAPS using the proposed criteria for postnatal diagnosis of TAPS, namely: Hb difference > 8 g/dL and very small intertwin anastomoses [4,16].

2.2. Processing of the placenta and determination of placental intertwin color (redness) concordance

Processing and gross examination of the placenta, including injection and categorization of the chorionic vasculature, was performed as previously described in detail [3,6,21]. The intertwin placental redness ("color") concordance was determined by computer-assisted analysis of digital images of the basal plate of each placental share, according to methods described by Tollenaar et al. [19]. Briefly, digital images were converted to the red spectrum channel using a freely available image analysis program, Image J (http://imagej.nih.gov), The placental shares of each twin were traced manually. For each placental share, a histogram of redness intensity was generated. In these redness intensity histograms, the x-axis represents the continuous red color scale (with intensity values ranging between 0 and 255), and the y-axis represents the number of pixels with that specific color intensity. In accordance with Tollenaar et al. [19], the intertwin placental redness difference was expressed as the color difference ratio (CDR). The CDR was calculated by dividing the mode of the color intensity histogram with the higher peak (paler share) by the mode of the color intensity histogram with the lower peak (more red share). Fig. 1 displays a representative color-discordant twin placenta with associated color intensity histograms.

2.3. Statistical analysis

Values are expressed as mean ± standard deviation (SD) or median (range). The significance of differences between groups was determined by Student *t*-test, Mann-Whitney *U* test, ANOVA with post-hoc Scheffe test, or Fisher's exact test, where applicable. Data were analyzed and graphically represented using GraphPad Prism 5 software (GraphPad Software Inc., San Diego, CA). A *P* value of < 0.05 was considered significant. The study was approved by the Institutional Review Board.

3. Results

3.1. Determination of intertwin color difference ratio (CDR) in monochorionic twins

The color difference ratio (CDR) was determined in a consecutive cohort of eligible non-TTTS diamniotic-monochorionic twin placentas for which choriovascular injection results and digital images of basal plate were available. A total of 148 monochorionic multiple placentas were examined between 2010 and 2016. Of these 148 cases, 48 were excluded for the following reasons: remote fetal demise (N = 10), TTTS (N = 5), delivery at <23 weeks gestation (N = 4), higher order multiple gestation (N = 5), monoamnionicity (N = 12), lack of photographic documentation of the basal plate (N = 4), lack of choriovascular injection (N = 6), or large amounts of adherent blood clot (N = 2). The intertwin CDR in the remaining 100 eligible non-TTTS diamniotic-monochorionic twin placentas ranged between 1.00 and 3.58 (median CDR: 1.14) (Fig. 2A); the 90th percentile of the CDR values in this cohort was 1.98.