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Chapter 3

Placental characteristics in monochorionic twins with spontaneous versus post-laser twin anemia polycythemia sequence

Abstract

Introduction:

Twin anemia-polycythemia sequence (TAPS) may occur in monochorionic twins either spontaneously or after laser surgery for twin-twin transfusion syndrome. Our aim was to analyze the placental angioarchitecture in spontaneous versus post-laser TAPS.

Methods:

We included all monochorionic twin placentas with spontaneous or post-laser TAPS injected at our center between 2002 and 2012. Placental angioarchitecture was evaluated using colored dye injection.

Results:

A total of 600 monochorionic placentas were injected during the study period of which 43 (7.2%) with TAPS (spontaneous TAPS, n=16; post-laser TAPS, n=27). Almost all anastomoses (96%; 119/124) were very small (diameter <1 mm) and the majority was localized near the placental margin. The median number of anastomoses per placenta was 4 (interquartile range (IQR): 3-5) in the spontaneous TAPS group and 2 (IQR: 1-3) in the post-laser TAPS group ($p = 0.003$). Arterio-arterial (AA) anastomoses were detected in 14.0% (6/43) of TAPS placentas and were all minuscule (diameter <1 mm). The rate of AA anastomoses in the spontaneous TAPS group and post-laser TAPS group was 18.8% (3/16) and 11.1% (3/27), respectively ($p = 0.184$).

Discussion:

Spontaneous TAPS placentas have a significantly higher total number of anastomoses compared to post-laser TAPS placentas. Most anastomoses were localized near the margins of the placenta. Minuscule AA anastomoses were detected sporadically in both groups and the rate of AA anastomoses is slightly higher in the spontaneous TAPS group than in the post-laser group.

Conclusion:

Spontaneous TAPS placentas have a different placental angioarchitecture than post-laser TAPS placentas in terms of number and type of vascular anastomoses.

Introduction

Twin anemia-polycythemia sequence (TAPS) is a rare form of feto-fetal transfusion and can be diagnosed ante- and postnatally. Antenatal diagnosis is based on predefined Doppler ultrasound criteria [1]. Postnatal diagnosis uses hematological criteria (chronic anemia with an increased reticulocyte count in the donor and polycythemia in the recipient) in combination with placental injection studies [2,3].

The typical angioarchitecture in TAPS placentas demonstrates only a few, minuscule and mostly unidirectional arterio-venous (AV) anastomoses [2,4]. Arterio-arterial (AA) anastomoses are rare and have, when present, a very small diameter [2,5]. TAPS can occur spontaneously in uncomplicated monochorionic (MC) twin pregnancies or after laser treatment for twin-to-twin transfusion syndrome (TTTS). The spontaneous form occurs in 3-5% of monochorionic pregnancies, while the post-laser form complicates 2-13% of TTTS pregnancies treated with laser coagulation [2,6-9]. Both forms of TAPS are characterized by the presence of large intertwin hemoglobin discordances without amniotic fluid discordances that are needed to diagnose TTTS [2]. Whether both forms have different clinical outcomes and different placental angioarchitecture has not been studied yet.

The objective of this study was to estimate the number and types of placental anastomoses in placentas with spontaneous TAPS compared to placentas with post-laser TAPS.

Methods

All consecutive TAPS placentas examined at our center between June 2002 and October 2012 were included in this study. Our center is a tertiary national referral center for the management of complicated monochorionic twin pregnancies, including TTTS and TAPS. Cases with an incomplete placental injection study were excluded from the study. We compared the placental angioarchitecture in spontaneous TAPS cases with post-laser TAPS cases. Some of the placental data has been published previously [4,5,10].

For the purpose of this study, TAPS was diagnosed using the following proposed postnatal criteria. An inter-twin hemoglobin difference >8.0 g/dl and at least one of the following: reticulocyte count ratio >1.7 or placenta with only small (diameter < 1 mm) vascular anastomoses [2]. Hemoglobin levels and reticulocyte count are routinely measured at birth in all monochorionic twins.

Each monochorionic placenta examined at our center is routinely injected with colored dye according to a previously described protocol [11]. After colored dye injection, placentas are photographed in a plain view, and digital pictures are saved for computer analysis. Data on placenta angioarchitecture, including the number, type and size of anastomoses and the percentage of placental territory are recorded and entered in a dedicated database. We also recorded the type of abnormal umbilical cord insertion, velamentous or marginal insertion (within 1 cm of the placental margin). Combination insertions are the combination of cord insertions of one placenta. The term peripheral is used in this context to indicate both marginal and velamentous insertions. The insertion-diameter ratio is the ratio between the distance between the two cord insertions and the maximum diameter of the placenta.

We measured the distance between each anastomosis and the margin of the placenta, and expressed this distance as a percentage of the distance between margin and center of the vascular equator. We divided the distance between margin and center of the vascular equator into 5 equal segments (of 20%), as previously reported [10]. Diameters of the anastomoses and individual placental territories were measured using ImageJ 1.45s (ImageJ, National Institutes of Health, USA).

Results of continuous variables were analyzed using ManneWhitney U test and categorical variables were analyzed with Fischer exact test. A p-value <0.05 was considered to indicate statistical significance. All statistical data were analyzed using IBM SPSS Statistics v20.0 (SPSS Inc., an IBM Company, Chicago, IL, USA).

Results

During the 10-year study period, 410 TTTS cases were treated with laser surgery at our center and we were able to examine 65% (265/410) of the lasered placentas. In the TTTS group treated with laser, 27 cases (10%) fulfilled the postnatal criteria for TAPS and were included in the post-laser group. During the same study period, 335 monochorionic placentas without TTTS were also examined at our center. In this group, 16 cases (5%) fulfilled the postnatal criteria for TAPS and were included in the spontaneous TAPS group. In total, 43 placentas fulfilled the inclusion criteria for postnatal TAPS and were included in the study (post-laser TAPS group, n=27; spontaneous TAPS group, n=16). Sixteen (37%) of these cases were also detected antenatally.

In the post-laser TAPS group, 5/27 (18.5%) pregnancies were treated with intrauterine

transfusion (IUT) or intraperitoneal transfusion. In the spontaneous TAPS group, 3/16 (18.8%) pregnancies were treated with intrauterine transfusion or intraperitoneal transfusion. Median gestational age at delivery was 33.5 weeks (interquartile range (IQR): 31-35 weeks) and 33 weeks (IQR: 29-34 weeks) in the spontaneous TAPS group and post-laser TAPS group, respectively (p = 0.038). Median inter-twin hemoglobin difference in the spontaneous and post-laser TAPS group was 14.2 g/dL and 12.2 g/dL, respectively (p = 0.784). Further details on the baseline characteristics are shown in Table 1.

	MC twins with spontaneous TAPS (n=32)	MC twins with post-laser TAPS (n=54)
Female n/N(%)	14/32 (44)	18/54 (33)
Gestational age at delivery - weeks [a]	33.5 (31-35)	33 (29-34)
Birth weight - grams [a]	1905 (1489-2109)	1701.5 (1189-2001)
Birth weight smaller twin - grams [a]	1750 (1181-1968)	1520 (1156-1770)
Birth weight larger twin - grams [a]	2020 (1556-2346)	1880 (1237-2140)
Birth weight discordance - % [a]	15.6 (8.3-26)	13.6 (4-20.8)
Caesarean delivery - n/N(%)	14/32 (44)	30/54 (56)
Inter-twin hemoglobin difference - g/dl [a]	14.2 (11.8-19.4)	12.2 (10.3-15.8)

[a] Value given as median (IQR).

Table 1: Baseline characteristics in MC placentas with spontaneous and post-laser TAPS.

A total of 124 anastomoses were detected. Of all anastomoses, the vast majority 96% (119/124) had a diameter <1 mm. Median total number of anastomoses in the spontaneous TAPS group and post-laser TAPS group was 4 anastomoses (IQR: 3-5) and 2 anastomoses (IQR: 1-3), respectively (p = 0.003). AV anastomoses were present in all (43/43) placentas. AA anastomoses were present in only 14% (6/43) of TAPS placentas and were detected in 18.8% (3/16) of spontaneous TAPS placentas compared to 11.1% (3/27) of postlaser TAPS placentas.

Median diameter of the AA anastomosis diameter in the spontaneous and post-laser TAPS groups was 0.4 mm and 0.6 mm, respectively (p = 0.184). All AA anastomoses (6/6) had a diameter <1 mm. Veno-venous (VV) anastomoses were detected in only 2 post-laser TAPS placentas (2/27; 7.4%) and in none of the spontaneous TAPS placentas. Detailed information of placental angioarchitecture is shown in Table 2.

In the spontaneous TAPS group, we found that in 75% (12/16) of placentas, AV anastomoses from donor to recipient were accompanied by VA anastomoses in opposite direction (from

	MC placentas with spontaneous TAPS (n=16)	MC placentas with post-laser TAPS (n=27)	p value
Number of anastomoses per placenta [a]	4(3-5)	2 (1-3)	0.003
AA anastomoses present (%)	3 (18.8)	3 (11.1)	0.184
VV anastomoses present (%)	0 (0)	2 (7.4)	0.522
AV anastomoses present (%)	15 (100)	27 (100)	1.00
Diameter of AA anastomosis (mm) [b]	0.4 (0.3-0.6)	0.6 (0.5-0.8)	0.184
Placental share discordance (%) [a]	29.7 (12-46)	20.1 (10.7-37)	0.688
Velamentous cord insertion - n(%) [c]	3/32 (9.4)	12/54 (22)	0.153
Marginal cord insertion - n(%) [c]	11/32 (34.4)	19/54 (35.2)	1.00
Velamentous or marginal cord insertion - n(%) [c]	14/32 (43.8)	31/54 (57.4)	0.267
Combination insertion [d]			
Peripheraleperipheral present (%)	5 (31.3)	6 (22.2)	0.719
Peripheralecentral present (%)	5 (31.3)	19 (70.4)	0.025
Centralecentral present (%)	6 (37.5)	2 (7.4)	0.037
Insertion-diameter ratio [a]	74 (60.1-87.6)	70 (59.3-76.7)	0.291

AA: arterio-arterial; VV: veno-venous; AV: arterio-venous.
[a] Value given as median (IQR).
[b] Value given as median (range).
[c] Refers to the type of cord insertion per fetus.
[d] Refers to the combination of cord insertion on one placenta.

Table 2: Placental characteristics in MC placentas with spontaneous and post-laser TAPS.

recipient to donor) or by bidirectional AA anastomosis. In the postlaser TAPS group, this combination occurred in only 37% (10/27) of cases. Compensating VA anastomoses or AA anastomoses occurred significantly more frequently in the spontaneous TAPS group than post-laser TAPS group (75% versus 37%, $p < 0.01$).

Velamentous or marginal cord insertions were present in 43.8% (14/32) and 57.4% (31/54) of spontaneous and post-laser TAPS twins respectively. The combinations of umbilical cord insertions and insertion-diameter ratio in both groups are presented in Table 2.

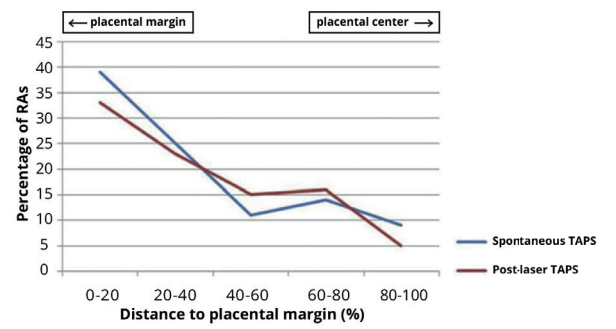

Figure 1. Distance of the anastomoses in relation to the margin of the placenta.

In both the post-laser TAPS group and spontaneous TAPS group, the localization of anastomoses was mostly close to the placental margin (Fig. 1). An example of a post-laser and a spontaneous TAPS placenta is shown in Figs. 2 and 3.

Discussion

TAPS placentas are characterized by the presence of few minuscule AV anastomoses and the rare occurrence of AA anastomoses [2]. This study shows that the unique placental angioarchitecture involved in the pathogenesis of TAPS is present in both spontaneous and post-laser TAPS. However, spontaneous TAPS placentas have a significantly higher total number of anastomoses compared to post-laser TAPS placentas. The discordance in number of anastomoses is probably related to the difference between both TAPS groups. Post-laser TAPS is an iatrogenic de novo event developing because one or two small anastomoses are left patent during surgery.

In addition, the rate of AA anastomoses appeared to be higher in the spontaneous TAPS group (18.8%) than in the post-laser group (11.1%), although the difference was not significant. Given the small numbers of included cases (which is inherent to the rarity of TAPS in general), lack of significance could be due to the fact that the study may be underpowered. Larger studies are required to determine reliably whether there is a difference in percentage

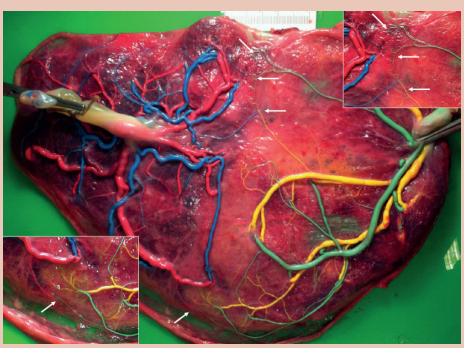

Figure 2. Spontaneous TAPS placenta after colored dye injection (blue or green for arteries and pink or yellow for veins). The placenta share on the right side of the picture belongs to the anemic donor and the placenta share on the left side belongs to the recipient. The white arrows indicate the AV and VA anastomoses. Details of the anastomoses are shown in the top-right and bottom-left corner.

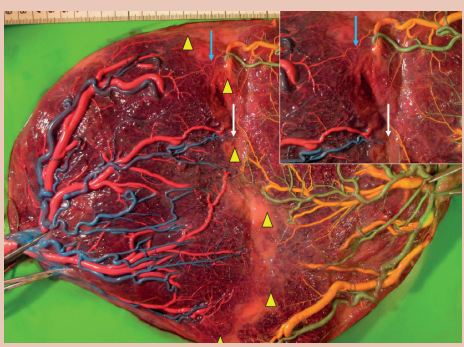

Figure 3. Post-laser TAPS placenta after colored dye injection lasered at 24 weeks' gestation and delivered at 37 weeks' gestation. The placenta share on the right side of the picture belongs to the anemic donor and the placenta share on the left side belongs to the recipient. The white arrow indicates an AV anastomosis and the blue arrow shows a VV anastomosis. The yellow cones show laser spots. Details of the anastomoses are shown in the top-right corner.

of AA between spontaneous TAPS cases and post-laser TAPS cases.
This study confirms that AA anastomoses are detected only in a minority of TAPS cases (14%, 6/43) and all AA anastomoses had a minuscule diameter (1 mm). The combination of few small AV anastomoses and sporadic small AA anastomoses is of paramount importance in the understanding of the pathophysiology of TAPS. These small anastomoses allow only a limited and slow transfer of blood from donor to recipient causing the large inter-twin hemoglobin difference in TAPS, but no oligo-polyhydramnios sequence. The volume of fluid passing through small anastomoses is less than in larger anastomoses as a result of an increased vascular resistance (Poisseuille's law). Discordant hemoglobin levels are therefore caused by the slow inter-twin blood transfusion (as low as 5-15 ml/ 24 h) [12-14]. This allows more time for compensatory hemodynamic regulation systems to act and probably prevents the development of hormonal imbalance and twin oligo-polyhydramnios sequence such as in TTTS [12-14].

We found that AV anastomoses in both directions (from donor to recipient and vice versa) or bidirectional anastomoses are more frequently present in spontaneous TAPS than post-laser TAPS placentas. This may explain why spontaneous TAPS cases may remain stable and undetected until the third trimester, whereas in postlaser TAPS a rapid decompensation occurs a few weeks after the intervention.

This study also shows that (residual) anastomoses (RA) in postlaser TAPS cases are usually found on the margin of the placenta, as previously also reported [10]. Interestingly, we found the same trend of higher rates of anastomoses nearer to the placental margin compared to the placental center in the spontaneous TAPS group. The increased rate of residual anastomoses in the post-laser group is thought to result from increased technical difficulties during fetoscopy to accurately visualize the complete vascular equator. The reason for the increased rate of anastomoses near the placental margin in the spontaneous TAPS group is not known. Whether this unequal spread of anastomoses differs from other monochorionic placentas with or without TTTS is not known either, as the localization of anastomoses has not yet been studied in monochorionic placentas.

The optimal management of TAPS is not clear and includes expectant management, intrauterine blood transfusion and fetoscopic intervention to coagulate the vascular anastomoses [1,2,8,15-17]. The clinical implication of the findings in this study is that if fetoscopic laser coagulation is envisaged, most of the few anastomoses in post-laser TAPS and spontaneous TAPS cases are found near the margins of the placenta. Since these anastomoses are extremely small and difficult to detect, laser coagulation of the complete

equator (Solomon technique) [2] would probably be the preferred laser technique. However, more studies (ideally randomized controlled trials) are required to determine the best treatment intervention in TAPS cases.

In conclusion, this comparative study between spontaneous TAPS and post-laser TAPS cases shows that post-laser TAPS cases have fewer anastomoses, less AA anastomoses and most anastomoses are localized near the margins of the placenta.

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