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Knijnenburg, P.J.C.; Slaghekke, F.; Tollenaar, L.S.A.; Gijtenbeek, M.; Haak, M.C.; Middeldorp, J.M.; ...; Lopriore, E.

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OBSTETRICS

Prevalence, risk factors, and outcome of postprocedural amniotic band disruption sequence after fetoscopic laser surgery in twin-twin transfusion syndrome: a large single-center case series

Check for updates

Patricia J. C. Knijnenburg, MD; Femke Slaghekke, MD, PhD; Lisanne S. A. Tollenaar, BSc; Manon Gijtenbeek, MD; Monique C. Haak, MD, PhD; Johanna M. Middeldorp, MD, PhD; Frans J. C. M. Klumper, MD; Jeanine M. M. van Klink, PhD; Dick Oepkes, MD, PhD; Enrico Lopriore, MD, PhD

BACKGROUND: Postprocedural amniotic band disruption sequence is a condition that is associated with intrauterine interventions, and it is characterized by a constriction of the limbs or umbilical cord by fibrous strands, leading to edema, amputation, and/or fetal demise.

OBJECTIVE: To evaluate the prevalence of, risk factors for, and the outcome of postprocedural amniotic band disruption sequence after fetoscopic laser surgery in twin-twin transfusion syndrome cases.

STUDY DESIGN: All consecutive cases of twin-twin transfusion syndrome treated with fetoscopic laser coagulation of the vascular anastomoses at our center between January 2002 and March 2019 were included in the study. The occurrence of postprocedural amniotic band disruption sequence in these cases was recorded, and the potential risk factors were analyzed.

RESULTS: Postprocedural amniotic band disruption sequence was detected, at birth, in 2.2% (15/672) of twin-twin transfusion syndrome cases treated with fetoscopic laser surgery, in both the recipients (10/15, 67%) and the donors (5/15, 33%). Postprocedural amniotic band disruption sequence primarily affected the lower extremities (11/15, 73%) and, less frequently, the upper extremities (2/15, 13%), both the upper and lower extremities (1/15, 7%), or the umbilical cord (1/15, 7%).

Postprocedural amniotic band disruption sequence led to the amputation of toes in 5 of 15 cases (33%) and resulted in fetal demise because of constriction of the umbilical cord in 1 case (7%). The independent risk factors identified for postprocedural amniotic band disruption sequence were lower gestational age at laser surgery (odds ratio per week, 1.43; 95% confidence interval, 1.12–1.79; P=.003) and the presence of postprocedural chorioamniotic membrane separation on antenatal ultrasound examination (odds ratio, 41.66; 95% confidence interval, 5.44–319.25; P<.001).

CONCLUSION: The prevalence of postprocedural amniotic band disruption sequence is low, but, when present, it may lead to severe consequences, with amputation of extremities or fetal demise occurring in more than one-third of the cases. Lower gestational age at the time of laser therapy and chorioamniotic membrane separation are independent risk factors for the postprocedural amniotic band disruption sequence.

Key words: chorioamniotic membrane separation, fetoscopic laser surgery, postprocedural amniotic band disruption sequence, twin-twin transfusion syndrome

A mniotic band syndrome is a fetal condition in which strands of the amniotic membrane encircle digits, limbs, or the umbilical cord of a fetus, leading to edema, hypoplasia, amputation, or even fetal death. The reported prevalence of amniotic band syndrome ranges from 1:1200 to 1:15,000 of live births.¹ Postprocedural amniotic band disruption

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sequence (PABDS) is a rare iatrogenic complication that is associated with invasive intrauterine procedures such as amniocentesis, amnioreduction, tracheal occlusion for congenital diaphragmatic hernia, thoracoamniotic shunt placement, and fetoscopic laser therapy in twin-twin transfusion syndrome $(TTTS).^{2-7}$ Because this is a rare complication, the amount of data available on PABDS in TTTS cases treated with laser therapy is limited, and the identification of possible risk factors is based on a small number of series or casuistic reports. Several potential risk factors for PABDS in TTTS have been described and include preterm premature rupture of membranes (PPROM) and inadvertent septostomy.^{7,8}

The aims of this study were to describe the occurrence of PABDS after fetoscopic laser surgery from a consecutive cohort of TTTS cases at our center, with specific focus on the prevalence, risk factors, and outcome, and to summarize the findings reported in the literature on PABDS.

Materials and Methods

All consecutive cases of TTTS treated with fetoscopic laser surgery at the Leiden University Medical Center (LUMC) between January 2002 and March 2019 were included in this cohort study. Patients' medical charts and ultrasound findings were reviewed for the presence of PABDS. Some of the data on PABDS in this cohort have already been reported in a previous publication in 2014.⁹ The LUMC is the national referral center for fetal therapy in the Netherlands. The study was approved by the Medical Ethics Committee of the LUMC. We confirmed the presence of PABDS either

AJOG at a Glance

Why was this study conducted?

The aims of this study were to describe the prevalence of and report risk factors for postprocedural amniotic band disruption sequence (PABDS) in a relatively large cohort of twin-twin transfusion syndrome (TTTS) cases that were treated with fetoscopic laser surgery.

Key findings

- The prevalence of PABDS after fetoscopic laser surgery in TTTS was 2.2%.
- The presence of amniotic bands frequently leads to amputations (mostly of digits) or to fetal demise when constriction involves the umbilical cord.
- Laser surgery during early gestation and chorioamniotic membrane separation were identified as independent risk factors for the occurrence of PABDS.

What does this add to what is known?

- This study reports on the largest case series of PABDS after fetoscopic laser surgery in TTTS and shows that although the prevalence is low, the risk of adverse outcome is high.
- The results from this study suggest that chorioamniotic membrane separation and early gestational age at fetoscopy are independent risk factors for PABDS.

sonographically by the detection of endangered blood flow or soft-tissue changes such as constriction, edema, or amputation or postnatally by the presence of constriction rings, edema, or amputation. In the case of autoamputation, PABDS was confirmed when an encircling band was present on the affected body appendage.

We excluded cases with incomplete medical records regarding delivery and neonatal outcome. The following variables were collected from ultrasound records, operation reports, and discharge letters: TTTS stage, gestational age at laser treatment, laser technique used (Selective or Solomon), procedure-related rupture of the intertwin membrane leading to iatrogenic monoamnionicity, PPROM before 32 weeks of gestation, ultrasound reports of chorioamniotic membrane separation, limb edema, disrupted blood flow to the limbs or in the umbilical cord and signs of limb amputation, presence and location of the amniotic bands (detected either antenatally by ultrasound or after delivery), donor or recipient status of the fetus, intrauterine fetal demise (IUFD), and gestational age at birth.⁹ We defined iatrogenic monoamnionicity either as a perforation of the intertwin

membrane detected during the laser procedure or at ultrasound examinations during a follow-up, or as cord entanglement observed during an antenatal ultrasound or at delivery. We defined chorioamniotic membrane separation as a separation of the amnion and chorion observed in at least 1 postprocedural ultrasound examination.

TTTS was defined according to the Eurofoetus criteria for amniotic fluid discordance: polyhydramnios in the recipient sac, identified by a deepest vertical pocket (DVP) of at least 8 cm before 20 weeks of gestation and at least 10 cm after 20 weeks of gestation, and oligohydramnios in the donor sac with a DVP of maximum 2 cm at any gestational age.¹⁰ The stages of TTTS were determined according to the internationally accepted criteria.¹¹ Fetoscopic laser surgery was performed using a 1.0-, 1.3-, or 2.0-mm fetoscope (Karl Storz, Tuttlingen, Germany) and an 8 or a 10 French cannula with a 400- μ m laser fiber (Dornier MedTech, Wessling, Germany or Tobrix Professional Medical Equipment, Waalre, the Netherlands) connected to a diode or Nd:YAG laser device (Dornier MedTech, Wessling, Germany).

A search of the literature up to December 2019 was carried out in PubMed using the Medical Subject Heading terms "amniotic band syndrome" and "fetofetal transfusion." Articles were included when they were published in English, reported cases of amniotic bands that were present after laser surgery for TTTS, and included sufficient clinical details such as gestational age at laser surgery, gestational age at birth, and location of the amniotic bands. Articles with insufficient clinical details or TTTS cases treated with other interventions were excluded. The overall median gestational age at the time of laser treatment and at the time of birth, the proclivity of PABDS to affect one fetus over the other (donor vs recipient), the fetal limbs most often affected, and the possible risk factors were determined by combining the data from the cases at our center and from the cases reported in literature.

Continuous variables were reported as the mean \pm standard deviation or as the median (interquartile range [IOR]). A chi-square test or Fisher exact test was used to compare proportions. The potential risk factors for amniotic band syndrome were analyzed using logistic regression analysis, and the variables from a univariate analysis with a *P* value less than .05 were included in the multivariate analysis. The following risk factors were included in the risk factor analysis: gestational age at laser treatment, PPROM before 32 weeks of gestation, iatrogenic monoamnionicity, postprocedural chorioamniotic and membrane separation. The correlation was calculated using a Pearson or Spearman rank correlation depending on the distribution of the continuous data. Statistical analysis was performed using SPSS Statistics version 25 (IBM SPSS Statistics for Windows, Version 25.0, IBM Corp, Armonk, NY).

Results

Between January 2002 and March 2019, 733 pregnancies treated with fetoscopic laser therapy for TTTS were eligible for inclusion in the study, with 381 (55%) of these delivered at our center and 311 (45%) delivered at the referring center.

TABLE 1 Detailed information about the PABDS cases from our center

Case	Affected fetus	Affected body part	GA at laser (wk)	GA at birth (wk)	Laser technique	IUFD	PPROM	latrogenic MA	Chorioamniotic membrane separation
1	Recipient	Left foot, digit I–V	16.4	22.6	Selective	Both ^a	Unknown	Yes	Yes
2	Donor	Left lower leg, left foot digit II, III, right foot digit II—V	15.0	29.7	Selective	No	Yes	No	Yes
3	Recipient	Right upper arm	18.0	27.3	Solomon	No No		No	Yes
4	Donor	"Toes"	17.7	33.6	Solomon	Recipient	Recipient No		Yes
5	Recipient	Right hand digit II	16.3	30.6	Solomon	No	lo Yes		Yes
6	Recipient	Left foot digit I-IV, right foot digit I, II, IV	17.0	33.1	Solomon	No	o No		Yes
7	Recipient	Both feet digit II—IV	17.9	29.3	Selective	No	No	No	Yes
8	Donor	Left foot digit I—III, right foot digit I-IV	17.0	35.9	Selective	No	No	No	Yes
9	Recipient	Right foot digit II—IV	17.0	36.4	Solomon	No	No	No	Yes
10	Donor	Umbilical cord	22.6	34.2	Solomon	Donor	No	No	Yes
11	Recipient	Left ankle	23.0	36.0	Solomon	No	No	No	Yes
12	Recipient	Right foot digit II—IV	16.9	36.3	Solomon	No	No	No	Yes
13	Donor	Right foot digit II—III	15.0	38.6	Selective	No	No	No	No
14	Recipient	Right ankle	16.0	30.6	Solomon	No	No	Yes	Yes
15	Recipient	Right foot digit III, IV, right hand digit I, left arm	16.2	36.4	Solomon	No	Unknown	No	Yes
Summary	Recipient 67%	Upper limbs 13% both 7% lower limbs 73% other 7%	17.0 (16.2—17.9)	33.6 (29.7—36.3)		20%	15%	20%	93%

Data are presented as median (interquartile range) or percentages.

GA, gestational age; IUFD, intrauterine fetal demise; MA, monoamnionicity; PABDS, postprocedural amniotic band disruption sequence; PPROM, preterm premature rupture of the membranes.

^a There were no bands on the umbilical cords.

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FIGURE 1 Amniotic band constricting umbilical cord of donor, leading to fetal demise



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In total, 61 (8%) cases, all of which were outborn, were excluded from the study because of incomplete data, and 672 cases (92%) were included in the study. A total of 15 cases (2.2%) of PABDS were identified, of which 33% (5/15) occurred in the donors and 67% (10/15) in the recipients (P=.21). All PABDS cases were detected only at birth and were not identified during antenatal ultrasound evaluations. In some cases, with extensive chorioamniotic membrane separation, the presence of amniotic bands was suspected, but this was, however, not confirmed antenatally. The characteristics of the affected cases are summarized in Table 1. Amniotic bands were located around the upper extremities in 13% (2/ 15) of the cases, around the lower

extremities in 73% (11/15) of the cases, around both the upper and lower extremities in 1 case (7%), and around the umbilical cord in 1 case (7%). In this last case (case 10), constriction of the cord by the amniotic band led to fetal demise (Figure 1). Amputation of limbs occurred in 5 of 15 cases (33%), and all involved the toes.

The risk factors for PABDS are summarized in Table 2. The median gestational age at laser surgery in the group with PABDS was lower compared with the group without PABDS, which was determined to be 17.0 (IQR, 16.2–17.9) weeks and 20.0 (IQR, 17.7–22.0) weeks, respectively (odds ratio [OR] per week, 1.43; 95% confidence interval [CI], 1.12-1.79; P=.003). In 14 of 15 (93%) cases of PABDS, chorioamniotic membrane separation was observed during antenatal ultrasound examinations compared with only 165 of 656 (25%) in the group without PABDS (OR, 41.66; 95% CI, 5.44-319.25; P<.001). In 7 of 14 (50%) of our PABDS cases with chorioamniotic membrane separation, the chorioamniotic membrane separation was detected in both sacs. In 6 of 14 cases (43%), the chorioamniotic membrane separation was detected in the sac of the affected twin, and in 1 of 14 cases (7%), it was detected in the sac of the unaffected twin. We found no difference in PPROM or iatrogenic monoamnionicity between the groups with or without PABDS. Chorioamniotic

membrane separation was correlated to early gestational age (in weeks) at laser surgery (correlation coefficient r, -0.16; P<.001). However, in the multivariate analysis, both chorioamniotic membrane separation and lower gestational age at laser surgery were independently associated with PABDS (OR, 32.90; 95% CI, 4.25–254.54; P=.001 and OR per week, 1.30; 95% CI, 1.03–1.61; P=.025, respectively).

Our literature search on the occurrence of PABDS after laser surgery as treatment for TTTS yielded a total of 24 articles. Eleven articles did not meet our inclusion criteria. In addition, 5 articles were excluded; 3 of these articles reported on PABDS cases without clinical details, and 2 reported on PABDS in TTTS cases that were treated with other interventions.^{4,8,12–14} Eight articles were eligible, yielding a total of 20 cases of PABDS with clinical details in 18 pregnancies; in 2 of the pregnancies both the donor and recipient were affected by PABDS.^{7,15–21} Adding the cases reported in our series yielded a total of 35 PABDS cases in 33 pregnancies. When we combined the cases in the literature (summarized in Table 3) with those in our series, most PABDS cases seemed to occur in the recipients (27/35, 77%). PABDS involved mostly the lower extremities (19/35, 54%) and, to a lesser extent, the upper extremities (8/35, 23%), both the upper and lower extremities (4/35, 11%), or the umbilical

TABLE 2 Risk factors for PABDS									
Characteristics	Amniotic band (n=15)	No amniotic band (n=657)	Univariate OR (95% CI)	<i>P</i> value	Multivariate OR (95% CI)	<i>P</i> value			
GA at laser, wk	17.0 (16.2–17.9)	20.0 (17.7–22.0)	1.43 (1.12–1.79)	.003	1.30 (1.03-1.61)	.025			
PPROM <32 wk	2/13 ^a (15)	195/654 ^b (30)	0.43 (0.09-1.95)	.273					
latrogenic monoamnionicity	3/15 (20)	115/654 ^b (18)	0.85 (0.24-3.07)	.808					
Chorioamniotic membrane separation	14/15 (93)	165/656 ^c (25)	41.66 (5.44-319.25)	<.001	32.90 (4.25-254.54)	.001			
	AL (0/)								

Data are presented as median (interquartile range) or n/N (%).

Cl, confidence interval; GA, gestational age; OR, odds ratio; PABDS, postprocedural amniotic band disruption sequence; PPROM, preterm premature rupture of the membranes.

^a Data for 2 cases were missing.; ^b Data for 3 cases were missing.; ^c Data for 1 case were missing.

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Overview of the PABDS cases reported in the literature										
Case	Affected fetus	Affected body part	GA at laser, wk	GA at birth, wk	Timing of detection	IUFD	PPROM	latrogenic MA	Chorioamniotic membrane separation	
1	Recipient	Both legs	21	26	2 Cases of 8	Donor	No	NA	NA	
2	Recipient	Left arm	23	34	Detected	Donor	No	NA	NA	
3	Recipient	Right leg	16	33.5	Antenatally	Donor	Yes	NA	NA	
4	Recipient	Right leg	21	30		Donor	Yes	NA	NA	
5	Recipient	Right foot	19	25.5		Donor	Yes	NA	NA	
6	Recipient	Left arm	19	33		Donor	No	NA	NA	
7	Recipient	Left arm	20	30		No	Yes	NA	NA	
8	Recipient	Right hand	16	31		Donor	Yes	NA	NA	
9	Recipient	Left foot dig I and II, right foot dig I—III	17	29	Postnatal	No	NA	NA	NA	
10	Donor	Left arm, digits left and right feet	16.4	39.7	Postnatal	Recipient	No	Possible	NA	
11	Recipient	Left foot dig I—III	16.6	33.1	Postnatal	No	No	No	NA	
12 ^a	Recipient	Right arm, left leg	18.9	29.3	Antenatal	Donor	No	Yes	NA	
13 ^a	Donor	Umbilical cord			Postnatal					
14	recipient	Left hand, dig I–III	18.3	26.1	Postnatal	Both	No	No	No	
15	Recipient	Face, umbilical cord	21.1	27.6	Postnatal	Recipient	Yes	No	Yes	
16	Recipient	Face, right hand dig I-IV, umbilical cord	16.1	30.7	Postnatal	Recipient	No	No	Yes	
17 ^a	Recipient	Right arm, ankle	18.0	27.0	Antenatal	Donor	Yes	Yes ^b	Yes	
18 ^a	Donor	Umbilical cord			Antenatal					
19	Recipient	Right foot, dig I	NA	NA	Postnatal	Donor	NA	No	NA	
20	Recipient	Right leg	NA	NA	Postnatal	No	NA	No	NA	
20	Recipient 85%		18.3 (16.5–20.5)	30.0 (27.0-33.1)	Antenatal detection 25%	78% (14/18)	44% (7/16)	25% (2/8)	75% (3/4)	
15	Recipient 67%		17.0 (16.2–17.9)	33.4 (29.7–36.3)	Antenatal 0%	20% (3/15)	15% (2/13)	20% (3/15)	93% (14/15)	
35	Recipient	77%	17.4 (16.3—19.0)	30.7 (28.0-34.2)	Antenatal 14%	53% (17/32)	31% (9/29)	22% (5/23)	89% (17/19)	
	Case 1 2 3 4 5 6 7 8 9 10 11 12 ^a 13 ^a 14 15 16 17 ^a 18 ^a 19 20 20 15 35	CaseAffected fetus1Recipient2Recipient3Recipient3Recipient4Recipient5Recipient6Recipient7Recipient8Recipient9Recipient10Donor11Recipient12aRecipient13aDonor14recipient15Recipient16Recipient17aRecipient18aDonor19Recipient20Recipient20Recipient15Recipient35Recipient	CaseAffected fetusAffected body part1RecipientBoth legs2RecipientLeft arm3RecipientRight leg4RecipientRight leg5RecipientRight foot6RecipientLeft arm7RecipientLeft arm8RecipientLeft arm9RecipientLeft foot dig I and II, right foot dig IIII10DonorLeft arm, digits left and right feet11RecipientReft ot dig IIII12RecipientRight arm, left leg13DonorUmbilical cord14recipientLeft hand, dig IIII15RecipientFace, umbilical cord16RecipientRight arm, ankle18DonorUmbilical cord17RecipientRight arm, ankle18DonorUmbilical cord17RecipientRight arm, ankle18DonorUmbilical cord19RecipientRight leg20RecipientRight leg20Recipient 8:5%15Recipient 6:7%	Affected fetusAffected body partGA at laser, wk1RecipientBoth legs212RecipientLeft arm233RecipientRight leg164RecipientRight leg215RecipientRight foot196RecipientLeft arm197RecipientLeft arm208RecipientRight hand169RecipientLeft foot dig I and II, right foot dig IIII1710DonorLeft arm, digits left and right feet16.411RecipientLeft foot dig IIII16.612 ^{e1} RecipientRight arm, left leg18.913 ^a DonorUmbilical cord21.114recipientEac, right hand dig 	Case Affected fetus Affected body part GA at laser, wk GA at birth, wk 1 Recipient Both legs 21 26 2 Recipient Left arm 23 34 3 Recipient Right leg 16 33.5 4 Recipient Right leg 21 30 5 Recipient Right foot 19 25.5 6 Recipient Left arm 20 30 7 Recipient Left foot 11 31 9 Recipient Right hand 16 31 9 Recipient Left foot dig I and II, right foot dig IIII 17 29 10 Donor Left arm, left leg 18.9 29.3 13 ^a Donor Umbilical cord 11.1 26.1 14 recipient Face, umbilical cord 21.1 27.6 14 recipient Face, right hand dig IIII 18.0 27.0 17 ^a Recipient<	CaseAffected fetusAffected body partGA at laser, wkGA at birth, wkTiming of detection1RecipientBoth legs21262 Cases of 82RecipientLeft arm2334Detected3RecipientRight leg1633.5Antenatally4RecipientRight leg2130	CaseAffected fetusAffected body partGA at laser, wkGA at birth, wkTiming of detectionIUFD1RecipientBoth legs21262 Cases of 8Donor2RecipientLeft arm2334DetectedDonor3RecipientRight leg1633.5AntenatallyDonor4RecipientRight leg2130	Affected fetusAffected body partGA at laser, wkGA at birth, wkTiming of detectionIUFDPPROM1RecipientBoth legs21262 Cases of 8DonorNo2RecipientLeft arm2334DetectedDonorNo3RecipientRight leg1633.5AntenatallyDonorYes4RecipientRight leg2130DonorYes5RecipientRight foot1925.5DonorNo6RecipientLeft arm1933DonorNoYes7RecipientLeft arm1933DonorNoYes8RecipientLeft arm1631DonorYes9RecipientLeft arm16.339.7PostnatalNoNo10DonorLeft arm, digits left and16.633.1PostnatalNoNo11RecipientLeft arm, left leg18.929.3AntenatalDonorNo12 ^a RecipientLeft hand, dig I-III18.326.1PostnatalNoNo13 ^a DonorUmbilical cord21.127.6PostnatalRecipientYes14recipientLeft hand, dig I-III18.326.1PostnatalBothNo15RecipientFace, right hand dig16.130.7PostnatalDonorYes16Recipient <t< td=""><td>Affected fetusAffected body partGA at laser, wkGA at laser, wkTiming of detectionIUFDPPROMMA1RecipientBoth legs21262 cases of 8DonorNoNA2RecipientIeff arm2334DetectedDonorNoNA3RecipientRight leg1633.5AntenatallyDonorYesNA4RecipientRight leg2130DonorYesNA5RecipientRecipientIeff arm1933DonorYesNA6RecipientLeft arm2030NoYesNA7RecipientRecipientRight hand1631DonorYesNA8RecipientRight nand16.331DonorYesNA9RecipientRight nand16.431.1DonorYesNa10DonorLeft arm, digits left and right feed16.433.1PostnatalNoNo11RecipientLeft foot dig I-III16.633.1PostnatalNoNoYes12*RecipientRight arm, left leg18.924.3AntenatalDonorYesNo12*RecipientRight arm, left leg18.924.3AntenatalDonorYesNo13*DonorUmbilical cord21.127.6PostnatalBothNoNo<td< td=""></td<></td></t<>	Affected fetusAffected body partGA at laser, wkGA at laser, wkTiming of detectionIUFDPPROMMA1RecipientBoth legs21262 cases of 8DonorNoNA2RecipientIeff arm2334DetectedDonorNoNA3RecipientRight leg1633.5AntenatallyDonorYesNA4RecipientRight leg2130DonorYesNA5RecipientRecipientIeff arm1933DonorYesNA6RecipientLeft arm2030NoYesNA7RecipientRecipientRight hand1631DonorYesNA8RecipientRight nand16.331DonorYesNA9RecipientRight nand16.431.1DonorYesNa10DonorLeft arm, digits left and right feed16.433.1PostnatalNoNo11RecipientLeft foot dig I-III16.633.1PostnatalNoNoYes12*RecipientRight arm, left leg18.924.3AntenatalDonorYesNo12*RecipientRight arm, left leg18.924.3AntenatalDonorYesNo13*DonorUmbilical cord21.127.6PostnatalBothNoNo <td< td=""></td<>	

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TABLE 3

Data are presented as median (interquartile range) or % (n/N).

GA, gestational age; IUFD, intrauterine fetal demise; MA, monoamnionicity; NA, not available; PABDS, postprocedural amniotic band disruption sequence; PPROM, preterm premature rupture of membranes.

^a Cases 12 and 13 and cases 17 and 18 are of the same twin pairs.; ^b After second procedure to release PABDS.; ^c Combined summary of the literature and the present cohort.

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FIGURE 2

Right foot of a recipient with amniotic bands constricting digits II, III, and IV



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cord (5/35, 14%) (Figure 2). PABDS led to amputation in 11 of 34 cases (32%), which only involved the fingers (2/11) or toes (9/11). Fetal demise occurred in all cases (5/5) in which amniotic strands were encircling the umbilical cord. Iatrogenic monoamnionicity was present in 5 of 23 (22%) of the cases with amniotic bands, whereas 9 of 29 (31%) cases had PPROM.

Comment Principal findings

We report here on the largest case series of PABDS occurrence after fetoscopic laser surgery for the treatment of TTTS. Our findings highlight that although PABDS is a rare complication with a prevalence of approximately 2%, it is associated with a high risk of amputation of fingers and toes or even fetal demise in cases of PABDS wherein the umbilical cord is constricted. Although limited by the relatively small sample size, risk factor analysis shows a possible association of PABDS with chorioamniotic membrane separation and early gestational age at laser treatment.

Clinical implications

The prevalence of PABDS in our study corroborates the results of previous studies

that reported a prevalence ranging from 1.5% to 3.3%.^{7-9,12} To date, 8 other smaller case series with clinical details of PABDS after fetoscopic laser therapy for TTTS have been reported in the literature.^{7,15–21} Adding the previously reported cases to the cases in our series yielded a total of 35 PABDS cases. There were some differences between our cohort and the smaller case series reported in the literature. These differences could possibly be explained by publication bias, as the published case reports described the more severe cases of PABDS, whereas milder cases often remain unpublished. In addition, the description of PPROM, perforation of the intertwin membrane, and chorioamniotic membrane separation in the literature was often incomplete, leading to underreporting bias. The true prevalence of the various risk factors is most probably higher than reported in this article.

Cruz-Martinez et al⁸ reported an association between the rupture of the intertwin membrane and PABDS (P<.001), with 50% (4/8) of PABDS cases in their study being iatrogenic monoamniotic. Winer et al⁷ reported an association between PPROM and PABDS (P=.05), as 63% (5/8) of the PABDS cases occurred in conjunction with PPROM before 33 weeks. These associations were not supported by the results of our study. Instead, our findings suggested that 2 other risk factors are associated with an increased risk of PABDS, namely chorioamniotic membrane separation and lower gestational age at laser surgery. As indicated in this study, chorioamniotic membrane separation was observed during prenatal ultrasound examinations in 93% (14/15) of PABDS cases compared with 25% (165/656) in pregnancies without PABDS. The overall prevalence of chorioamniotic membrane separation reported in this study is comparable to the 18.8% prevalence found in a recent study by De Zoysa et al.²² In addition, fetoscopic laser surgery was performed 3 weeks earlier in the group with PABDS compared with the average gestational age of 20 weeks in the group without PABDS. These findings suggest a possible relation between early gestational age at laser treatment and an increased risk of chorioamniotic membrane separation leading to PABDS. In general, the amniotic and chorionic membranes fuse after the first trimester, at approximately 14 weeks of gestation.²³ Hypothetically, fetoscopic intervention at an earlier gestational age may increase the risk of fetal membrane disruption, as the process of fusion is not completed, causing chorioamniotic membrane separation. The ruptured floating sheets of amnion may form strings and entrap the upper and lower extremities. In accordance with our results, Ortiz et al²⁴ and Takano et al²⁵ reported an increased risk of chorioamniotic membrane separation when fetoscopy occurred before 18 and 20 weeks of gestation, respectively (OR, 2.94; 95% CI, 1.64-5.28 and OR, 3.38; 95% CI, 1.44-7.93). A possible association between chorioamniotic membrane separation and PABDS after intrauterine interventions (eg, amniocentesis or fetoscopy for diaphragmatic hernia) has been hypothesized previously by Graf et al⁵ and Lewi et al.²⁶ To the best of our knowledge, this is the first study to show an association between chorioamniotic membrane separation and PABDS in TTTS after laser surgery. It is important to note that causation needs to be distinguished from mere association, and our study was not designed to evaluate a possible causal association.

This study also highlights the difficulty of antenatal detection of amniotic bands because all PABDS cases in our case series were only detected postnatally. Most amniotic bands in this study constricted either fingers or toes, with the arms or legs being affected only in a small number of cases. The presence of bands around fingers or toes are probably more difficult to detect sonographically than bands around an arm or a leg. This could explain why PABDS in this study was not diagnosed antenatally. This is in accordance with the literature, as accurate antenatal detection was reported in only 4 cases and fetoscopic surgical intervention to release the PABDS was performed in 2 cases. Timely prenatal detection of entrapped digits, limbs, or umbilical cords would allow for therapeutic fetoscopic intervention to release the amniotic bands. Gueneuc et al²⁷ reported that fetoscopic amniotic band release resulted in a functional limb in 70.4% (19/27) of the cases of twins and singletons with spontaneous or PABDS, based on data from their own center and from previous studies. However, reintervention has to be considered carefully for every individual case because fetoscopy may also increase the risk for other complications (such as PPROM or infection), thereby affecting the survival of and complications in both twins. Of note, Winer et al⁷ reported that PABDS occurred exclusively in the recipients. However, in our study, PABDS was detected in both donors and recipients. Increased awareness about the detection of PABDS antenatally through ultrasound should therefore not focus on recipients alone.

Strengths and limitations

The data from this study should be interpreted with caution, as bias may have been introduced because of the retrospective nature of the study and the potential risk of under- or overreporting. In addition, the limited sample size restricted the statistical analysis of various risk factors. We performed an explorative multivariate risk factor analysis, although the number of cases was too small to derive reliable conclusions about causation. Nevertheless, this is the largest case series of PABDS to date, and the combination of our data with the results of previous smaller series gives caregivers more reliable information on the prevalence of, risk factors for, and the outcomes of PABDS after fetoscopic laser surgery for TTTS.

Conclusion

PABDS is a rare but severe complication of fetoscopic laser surgery in TTTS cases that can lead to mutilations, amputations, or even fetal demise. We found that a low gestational age at laser surgery and chorioamniotic membrane separation were independently associated with an increased risk of PABDS. Increased awareness and limb surveillance using ultrasound, particularly in cases with early laser surgery or chorioamniotic membrane separation, may improve antenatal detection and possibly the likelihood of successful antenatal treatment.

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Author and article information

From the Division of Neonatology, Department of Pediatrics (Drs Knijnenburg and Lopriore); Division of Fetal Medicine, Department of Obstetrics (Dr Slaghekke, Ms Tollenaar, and Drs Gijtenbeek, Haak, Middeldorp, Klumper, and Oepkes); and Division of Child and Adolescent Psychology, Department of Pediatrics (Dr van Klink), Leiden University Medical Center, Leiden, the Netherlands.

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Corresponding author: Patricia J.C. Knijnenburg, MD. P.J.C.Knijnenburg@lumc.nl