CEOG Clinical and Experimental Obstetrics & Gynecology

Two-headed twin in a triplet pregnancy after in vitro fertilization – A case report and review of the literature

K. Lachowski[1], M. Lachowska[2], D. Paluszyńska[2], B. Królak-Olejnik[2]

[1]Students' Scientific Club of Neonatology, [2]Department of Neonatology, Wrocław Medical University, Wrocław (Poland)

Summary

Conjoined twins (CT) in triplet pregnancies are especially rare, approximately less than one in a million deliveries. *Purpose:* For better understanding of such malformations the authors performed a review of the literature published in the era of sonographic imaging, concerning CT in triplet gestations, as well as in the multiple pregnancies conceived by artificial reproduction (assisted reproductive techniques, ART). *Case Report:* A 26-year-old primigravida who underwent in vitro fertilization with embryo transfer (IVF-ET) was diagnosed with dichorionic, diamniotic triplet gestation. In the 33th week of pregnancy, a healthy male singleton was born, together with paraphagus dicephalus dibrachius dipus twins. *Results:* This is one of only a few cases reported in the literature of a lively born neonate with such malformations, its uniqueness even increased by the occurrence in triplet gestation conceived with ART. The literature reports three options for the triplet pregnancy with a CT: its continuation with an enhanced risk of premature delivery, termination of the entire gestation, or selective feticide of the CT. In the present case, although the defect was detected in the first trimester, no fetal reduction was performed and both infants were born alive. No intervention was deemed appropriate as the healthy singleton was uneventfully delivered and discharged home. *Conclusions:* ART, such as IVF-ET, are related to a higher prevalence of monozygotic twins, implying that the procedure might also increase the occurrence of CT. Notwithstanding the rarity of CT in triplets, such gestations are a significant challenge for the proper diagnosis and maintenance.

Key words: Conjoined twins; Triplet pregnancy; Artificial reproduction; In vitro fertilization.

Introduction

Conjoined twins (CT) are a type of monozygotic, monochorionic, and monoamniotic twins, created due to the anomalies in the physiological process of embryogenesis [1]. In the literature there are two theories related to the origin of this defect – fission and fusion theories respectively [1-4]. The first of them describes an unspecified mechanism according to which an embryo, during its fission, becomes trapped within the incompletely ruptured, pathologically inflexible zona pellucida. It is supposed that for the formation of the CT the division of the embryonic disc must occur relatively late, between 13th and 15th day after conception; therefore there is a risk for the embryoblast and trophoblast to remain connected [1, 4, 5]. The fusion theory on the other hand assumes that two monoamniotic embryonic discs can grow adjoining one to another at various angles, resulting in the their secondary unification – dorsal (through the neural tubes), ventral (through the mutual yolk sac) or lateral - symmetrical or asymmetrical, but always homologous union. It was discovered that mammalian embryos can be divided artificially in halves or quarters before compaction and survive. It is crucial to culture such split embryos in distinctly separate areas to avoid subsequent aggregation and formation of a single chimera [6, 7]. According to some of the authors, only this theory fully explains why the newborns can be joined by such diverse regions for whose the fusion is impossible in the early stages of embryogenesis [3, 8].

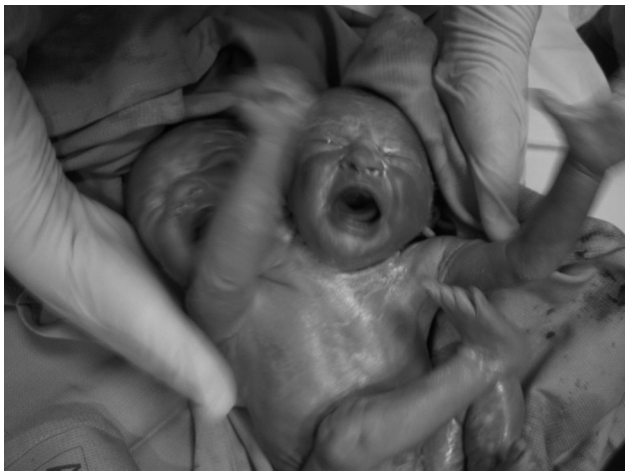
The frequency of conjoined twinning varies from one per 100,000 to 200,000 live births [9]. Such incidence in triplet pregnancies is especially rare, approximately less than one in a million deliveries [10]. About 40% of all CT undergo spontaneous intrauterine apoptosis and 35% of those who are lively born die in the first day [11]. Despite the rarity of their appearance, such gestations are a significant challenge for the gynaecologists and obstetricians, both due to the proper diagnosis as to the decision for the pregnancy maintenance [10]. Another difficulty lies beneath the assessment of the surgical possibility of separating the CT, however there are known examples of living twins.

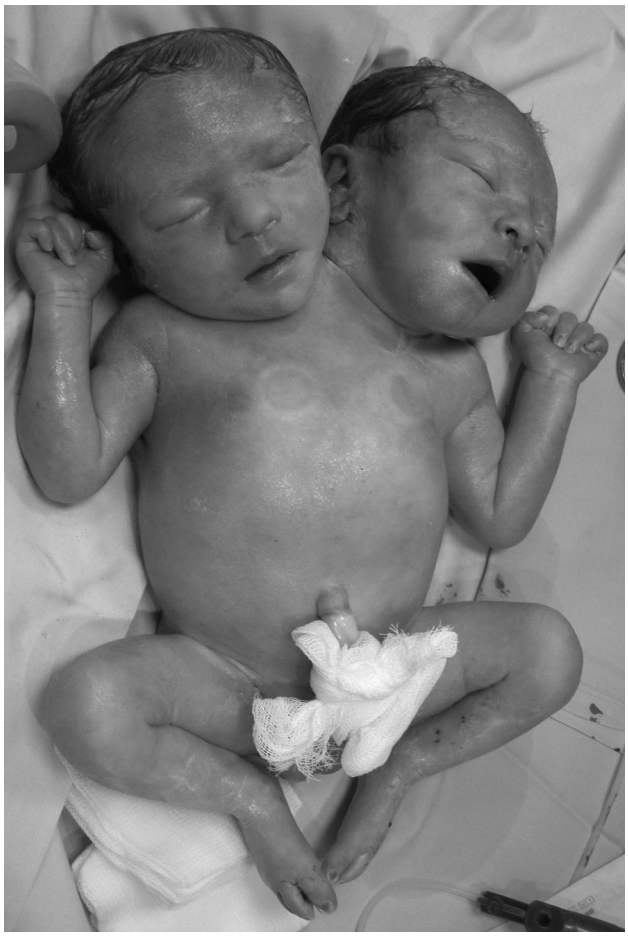
The purpose of this review was to determine the impact on the prenatal diagnosis as well as the usage of artificial reproduction techniques (ART) on the triplet gestations with CT, especially for the prognosis of the non-conjoined triplet. A PubMed search of the English-language literature was performed, using the tags 'conjoined twins', 'triplet pregnancy', 'artificial reproduction', and 'in vitro fertilization'.

Revised manuscript accepted for publication July 24, 2017

Clin. Exp. Obstet. Gynecol. - ISSN: 0390-6663
XLV, n. 5, 2018
doi: 10.12891/ceog4295.2018

7847050 Canada Inc.
www.irog.net





Figures 1 and 2 — Conjoined twins of paraphagus dicephalus dibrachius dipus type.

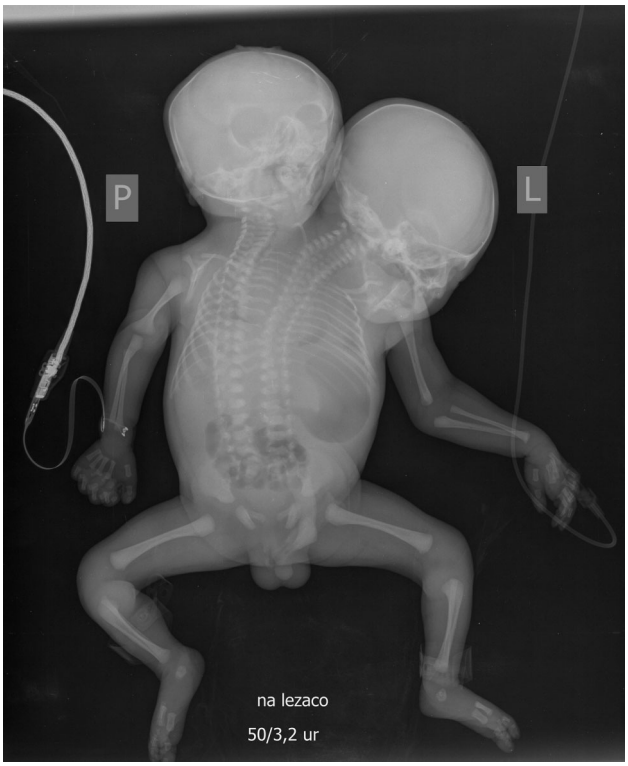


Figure 3. — An X-ray reveals the junction of spinal columns in the sacral area.

Case Report

In the beginning of December 2015, there was a 26-year-old female patient admitted to the Department of Obstetrics and Gynaecology of the University Hospital of Wrocław, Poland. She was in the 26th week of gestation and had a diagnosis of a dichorionic and diamniotic triplet gestation, with the presence of a pair of CT. The pregnancy was conceived after in vitro fertilization with embryo transfer (IVF-ET), in the 10th week of which in one of the gestational sacs the CT were diagnosed. The echocardiography of the fetuses revealed a complex heart malformation of the babies conjoined by their thoraxes. In the 33rd week of gestational age (wga), on January 18th 2016 the planned cesarean section was performed and a healthy male singleton was delivered together with CT in average condition, whose anatomy can be defined as paraphagus dicephalus dibrachius dipus (Figures 1 and 2). The twins were male, weighing 2,820 grams and scored 7/5/4/4 APGAR. After delivery the newborn was weepy, had peripheral cyanosis, and with weakened muscle tonus and reflexes. After two minutes breathing became irregular, but according to the prenatal neonatological consultation, no resuscitation was performed; palliative therapy was implemented instead. The twins were laid under the infant warmer, received analgetics, glucose infusion, and oxygen. Two hours and 21 minutes later, the decease due to the circulatory insufficiency was pronounced.

During the pregnancy in the 26th week, the perinatal cardiological consultation revealed a complex heart malformation: two aortae, one growing above the ventricular septal defect, two aortic arches joined into one vessel in the thoracic area, and two hypoplastic pulmonary trunks. Postnatal ultrasonography of the brain revealed asymmetry and intraventricular haemorrhage (IVH) of second degree. In the autopsy a diagnosis was made of separate lungs with hypoplastic medial lungs, two stomachs, one of them imperforated and two pancreases, moreover the cardiac malformation was confirmed. The rest of the abdominal organs were shared, the twins were conjoined by their ribs, there was also a junction of spinal columns observed in the sacral area, followed by the presence of individual pelvic bones (Figure 3). The diagnosis included full atelectasis of both lungs, effusion in both pleu-

Table 1. — Conjoined twins in triplet gestations and in the ART-conceived multiple pregnancies.

Case	Study	Age (yrs)	Parity	Gestational age at diagnosis	ART	Outcome	No. of fetuses
1	***Hartung et al. (1984)[10]***	21	0	N/K	No	Lively born by caesarean delivery, ROM and preterm labour	3
2	***Koontz et al. (1985)[10]***	32	2	29	No	Lively born by caesarean delivery in 31 wga, ROM and preterm labour	3
3	***Shalev and Zuckerman (1987)[10]***	36	4	21	No	Pregnancy termination 3	
4	***Apuzzio et al. (1988)[10]***	30	0	15	No	Pregnancy termination 3	
5	***Sakala et al. (1989)[10]***	19	1	17	No	Pregnancy termination 3	
6	***Lipitz et al. (1995)[10]***	25	1	16	No	Selective fetoreduction, intrauterine demise of the healthy fetus	3
7	***Gardeil et al. (1998)[10]***	34	2	13	No	Lively born by planned caesarean delivery in 36 wga	3
8	***Wax et al. (1999)[10]***	18	0	16	No	Pregnancy termination	3
9	***Sepulveda et al. Case 1 (2003)[10]***	41	2	13	No	Selective fetoreduction, intrauterine demise of the healthy fetus in 28 wga	3
10	***Sepulveda et al. Case 2 (2003)[10]***	29	2	10	No	Early demise of the CT, healthy fetus lively born at term	3
11	***Athanasiadis et al. (2004)[28]***	30	1	22	No	Pregnancy termination in 22 wga (conjoined triplets)	3
12	***Shepherd and Smith (2011)[29]***	32	0	13	No	Selective fetoreduction in 13 wga, healthy fetus lively born	3
13	*Rohilla et al. (2011)[30]*	N/K	N/K	1st trimester	No	N/K	4
14	***Kaveh et al. (2013)[31]***	27	1	15	No	Lively born by planned caesarean delivery in 36 wga	3
-	*ART Concieved Pregnancies:*	-	-	-	-	-	-
15	***Boulot et al. (1992)[12]***	27	0	10	Yes	Selective fetoreduction, healthy fetus lively born at term	3
16	***Skupski et al. (1995)[2]***	35	2	12	Yes	Selective fetoreduction, healthy fetus lively born at term	3
17	***Goldberg et al. (2000)[5]***	28	0	8	Yes	Selective fetoreduction, healthy fetus lively born at term	3
18	*Fujimori et al. (2004)[12]*	30	0	28	Yes	Intrauterine death	2
19	*Shimizu et al. (2004)[12]*	36	0	10	Yes	Pregnancy termination in 11 wga	2
20	*Mamyon et al. (2005)[12]*	37	1	12	Yes	Cesarean delivery in 38 wga	4
21	*Charles et al. (2005)[12]*	20	N/K	10	Yes	Preterm labour in 21 wga	2
22	*Allegra et al. (2007)[12]*	38	0	12	Yes	Cesarean delivery in 38 wga	4
23	*Mendilcioglu and Simsek (2008)[12]*	22	0	11	Yes	Cesarean delivery in 36 wga	4
24	*Hirata et al. (2009)[16]*	34	1	8	Yes	Vaginal delivery in 39 wga	2
25	*Poret et al. (2010)[12]*	30	0	9	Yes	Pregnancy termination in 11 wga	2
26	***Talebian et al. (2015)[23]***	38	0	13	Yes	Selective fetoreduction, intrauterine demise of the healthy fetus	3
27	***Our case (2016)***	26	0	10	Yes	Lively born by planned caesarean section in 33 wga	3

Table legend: bold – triplet pregnancies; *underlined – triplet pregnancies after ART.*

rae, and in the pericardium, morphological features of multiple organ immaturity, as well as the venal hyperaemia of the parenchymal organs.

Discussion

The antenatal procedures together with postnatal examination and autopsy allowed for the accurate description of the reported case. For better understanding of such malformations, the authors performed a review of the literature published in the era of ultrasound imaging, concerning conjoined twins occurring in triplet gestations, as well as in the ART-conceived multiple pregnancies. The comparison of reported pregnancies of such type (including the present case), together with their outcome, was made in the form of a table (Table 1), based on the ones previously made by Mercan *et al.* and Sepulveda *at al.* [10, 12].

Before the ultrasound became widely used in diagnosis, there were only nine cases of CT in triplet gestations published in the medical literature until 1971 [13]. The reported perinatal mortality rate was 89% for twins and 56% for normal triplets.

Monozygotic twinning (MZT) after IVF was first reported in 1984, and since then numerous studies have proved an increased incidence of MZT appearance accompanying the use of ART procedures [14, 15].

The singularity of the present case is due to its certain characteristics; firstly the CT appeared in a triplet gestation. In the era of sonographic imaging, according to what we have managed to discover until now, there are only 18 such cases described, including the present; among them only in case of five pregnancies ART procedures were used [10, 12, 16]. Secondly the present case describes the lively born CT of a very rare anatomical type [1]. The most common varieties are thoraco-omphalopagus (28%), thoracopagus (18.5%), and omphalopagus (10%) [17].

Due to these facts, a question arises: is it possible for ART to have an impact on the CT formation? Some of the authors claim that their usage enhances the frequency of the monozygotic twin appearance and moreover can be associated with the potential risk of conjoined twinning [18-20]. Such procedures as late ET, its delayed implantation or micromanipulations (for instance incision of the zona pellucida) can increase the occurrence of monozygotic twins [21, 22]. Conjoined twinning was indeed predicted when the zona pellucida incision technique called assisted hatching was first described [2, 23]. Prolonged in vitro culture may harden the zona pellucida, contributing to the formation of MZT. It is reported that high rate of MZT appeared after blastocyst stage transfer compared with a three day old ET [24]. It is related to the previously described risk of the embryo being trapped in the incompletely ruptured zona pellucida: it may get pinched off and divide, forming CT [19]. The occurrence of monozygotic fission is reported to be higher in gestations with two or more gestational sacs than that of the pregnancies with single one [20, 21]. Notwithstanding the reduction of the number of transferred embryos in ART procedures, the risk of higher-order multiple pregnancies is not eliminated [25].

In the literature there were cases reported of the CT appearance in pregnancies after IVF; considering the twin, triplet and quadruplet gestations, there were 13 such cases described, including the present [12, 25]. Due to the rarity of the CT occurrence, the research group is relatively small, hence it is difficult to define any conclusions concerning the relation between the CT and ART on its basis [16].

The review of the literature reveals three options for the triplet gestation with CT: its maintenance with the awareness of the high risk of premature delivery, the termination of the whole pregnancy, or the selective fetoreduction of the conjoined twins [10, 26, 27]. The lack of intervention is associated with an increased threat of preterm labour and perinatal decease of the non-conjoined triplet, while termination of the pregnancy implies its death. On the other hand selective termination, whose aim is to prevent complications for the normal fetus, is related to a miscarriage rate ranging from 5% to 10%, depending on the gestational age [26]. Clinical experience with second trimester selective termination indicates that the earlier the procedure is performed, the lower the loss rates are; furthermore the gestational age at delivery is greater as compared with later procedures [28, 29]. Moreover in monochorionic triplet gestations, the technical difficulties associated with placental vascular anastomoses arise. There is a risk of subsequent death or neurological sequelae for the normal fetus, as in the aforementioned case, its vessels are connected with the CT.

In the present case despite the defect was detected early (in first trimester), the decision of maintaining the pregnancy was made. This occurred correctly, as it enabled a proper development and delivery without complications for the healthy singleton, who was later discharged home together with his mother.

Conclusions

The widespread use of the ultrasound techniques allows for the early diagnosis of many fetal malformations, including CT. ART, such as IVF-ET, is related to a higher prevalence of monozygotic twins, implying that the procedure might also increase the occurrence of CT. Regardless of the rarity of their appearance in triplet gestations, they still pose a significant challenge for the proper diagnosis and the further maintenance of the pregnancy.

References

[1] Spencer R.: "Theoretical and analytical embryology of conjoined twins: part 1: Embryogenesis". *Clin. Anat.*, 2000, *13*, 36.
[2] Skupski D.W., Streltzoff J., Hutson J.M., Rosenwaks Z., Cohen J., Chervenak F.A.: "Early diagnosis of conjoined twins in triplet pregnancy after in vitro fertilization and assisted hatching". *J. Ultrasound Med.*, 1995, *14*, 611.
[3] Barth R.A., Filly R.A., Goldberg J.D., Moore P., Silverman N.H.: "Conjoined twins: prenatal diagnosis and assessment of associated malformations". *Radiology*, 1990, *177*, 201.
[4] Volpes A., Sammartano F., Coffaro F., Mistretta V., Scaglione P., Allegra A.: "Number of good quality embryos on day 3 is predictive for both pregnancy and implantation rates in in vitro fertilization/intracytoplasmic sperm injection cycles". *Fertil. Steril.*, 2004, *82*, 1330.
[5] Goldberg Y., Ben-Shlomo I., Weiner E., Shalev E.: "First trimester diagnosis of conjoined twins in a triplet pregnancy after IVF and ICSI". *Hum. Reprod.*, 2000, *5*, 1413.
[6] Nicholas J.S., Hall B.V.: "Experiments on developing rats. II. The development of isolated blastomeres and fused eggs". J. Exp. Zool., 1942, *90*, 441.
[7] Willadsen S.M.: "A method for culture of micromanipulatied sheep embryos and its use to produce monozygotic twins". *Nature*, 1979, *277*, 298.
[8] Spencer R.: "Theoretical and analytical embryology of conjoined twins: part 2: Adjustments to union". *Clin. Anat.*, 2000, *13*, 97.
[9] Rees A.E., Vujanic G.M., Williams W.M.: "Epidemic of conjoined twins in Cardiff". *Br. J. Obstet. Gynaecol.*, 1993, *100*, 388.
[10] Sepulveda W., Munoz H., Alcalde J.L.: "Conjoined twins in a triplet pregnancy: early prenatal diagnosis with three-dimensional ultrasound and review of the literature". Ultrasound Obstet. Gynecol., 2003, *22*, 199.
[11] Sellami A., Chakroun N., Frikha R., Bouayed N.A., Amouri H.,

Rebai T.: "Xipho-omphalopagus conjoined twins in a spontaneous triplet pregnancy: autopsy findings". *APSP J. Case Rep.*, 2013, *18*, 49.
[12] Mercan R., Oktem O., Salar Z., Nuhoglu A., Balaban B., Urman B.: "Conjoined twins after intracytoplasmic sperm injection and transfer of day-3 embryos". *Fertil. Steril.*, 2011, *96*, 111.
[13] Tan K.L., Tock E.P.C., Dawood M.Y., Ratnam S.S.: "Conjoined twins in a triplet pregnancy". *Am. J. Dis. Child.*, 1971, *122*, 455.
[14] Yovich J.L., Stanger J.D., Grauaug A., Barter R.A., Lunay G., Dawkins R.L., *et al.*: "Monozygotic twins from in vitro fertilization". *Fertil. Steril.*, 1984, *41*, 833.
[15] Aston K.I., Peterson C.M., Carrell D.T.: "Monozygotic twinning associated with assisted reproductive technologies: a review". *Reproduction*, 2008, *136*, 377.
[16] Hirata T., Osuga Y., Fujimoto A., Oishi H., Hiroi H., Fujiwara T., *et al.*: "Conjoined twins in a triplet pregnancy after intracytoplasmic sperm injection and blastocyst transfer: case report and review of the literature". *Fertil. Steril.*, 2009, *91*, e9.
[17] Kaufman M.H.: "The embryology of conjoined twins". Childs Nerv. Syst., 2004, *20*, 508.
[18] Wenstrom K.D., Syrop C.H., Hammit D.G., Van Voorhis B.J.: "Increased risk of monochorionic twinning associated with assisted reproduction". *Fertil. Steril.*, 1993, *60*, 510.
[19] Alikani M., Noyes N., Cohen J., Rosenwahs Z.: "Monozygotic twinning In the human is associated with the zona pellucida architecture". *Hum. Reprod.*, 1994, *9*, 1318.
[20] Derom C., Vlietinck R., Derom R., Van der B.H., Thiery M.: "Increased monozygotic twinning rate after ovulation induction". *Lancet*, 1987, *1*, 1236.
[21] Milki A.A., Jun S.H., Hinckley M.D., Behr B., Giudice L.C., Westphal L.M.: "Incidence of monozygotic twinning with blastocyst transfer compared to cleavage-stage transfer". *Fertil. Steril.*, 2003, *79*, 503.
[22] Sheiner E., Har-Vardi I., Potashnik G.: "The potential association between blastocyst transfer and monozygotic twinning". *Fertil. Steril.*, 2001, *75*, 217.
[23] Hershlag A., Paine T., Cooper G.W., Scholl G.M., Rawlinson K., Kvapil G.: "Monozygotic twinning associated with mechanical assisted hatching". *Fertil. Steril.*, 1999, *71*, 144.
[24] Tarlatzis B.C., Qublan H.S., Sanopoulou T., Zepiridis L., Grimbizis G., Bontis J.: "Increase in the monozygotic twinning rate after intracytoplasmic sperm injection and blastocyst stage embryo transfer". *Fertil. Steril.*, 2002, *77*, 196.
[25] Talebian M., Rahimi-Sharbaf F., Shirazi M., Teimoori B., Izadimood N., Sarmadi S.: "Conjoined twins in a monochorionic triplet pregnancy after in vitro fertilization: a case report". *Iran J. Reprod. Med.*, 2015, *13*, 729.
[26] Evans M.I., Goldberg J.D., Horenstein J., Wapner R.J., Ayoub M.A., Stone J., *et al.*: "Selective termination for structural, chromosomal and Mendelian anomalies: international experience". *Am. J. Obstet. Gynecol.*, 1999, *191*, 893.
[27] Sebire N.J., Sepulveda W., Jeanty P., Nyberg D.A., Nicolaides K.H.: "Multiple gestations". *In:* Nyberg D.A., McGahan J.P., Pretorius D.H., Pilu G., (eds). *Diagnostic Imaging of Fetal anomalies.* Philadelphia: Lippincott Williams & Wilkins, 2003, 777.
[28] Berkowitz R.L., Lynch L., Chitkara U., Wilkins I.A., Mehalek K.E., Alvarez E.S.: "Selective reduction of multifetal pregnancies in the first trimester". *N. Engl. J. Med.*, 1988, *318*, 1043.
[29] Wapner R.J., Davis G.H., Johnson A.: "Selective reduction of multifetal pregnancies". *Lancet*, 1990, *335*, 90.
[30] Athanasiadis A.P., Tzannatos C., Mikos T., Zafrakas M., Bontis J.N.: "A unique case of conjoined triplets". *Am. J. Obstet. Gynecol.*, 2005, *192*, 2084.
[31] Shepherd L.J., Smith G.N.: "Conjoined twins in a triplet pregnancy: a case report". *Case Rep. Obstet. Gynecol.*, 2011, *2011*, 235873.
[32] Rohilla S., Dahiya K., Rathee S., Yadav R.K., Dhaulakhandi D.B.: "Conjoined twins in a spontaneous trichorionic quadruplet pregnancy: a case report". *J. Reprod. Med.*, 2011, *56*, 351.
[33] Kaveh M., Kamrani K., Naseri M., Danaeian M., Asadi F., Davari-Tanha F.: "Dicephalic parapagus tribrachius conjoined twins in a triplet pregnancy: a case report". *J. Family Reprod. Health*, 2014, *8*, 83.

Corresponding Author:
K. LACHOWSKI, M.D.
ul. wyb. L. Pasteura 14/4
50-367 Wrocław (Poland)
e-mail: kplachowski@gmail.com