Tomasz Talar[1], Urszula Pacześniak[1], Marek Nowiczewski[1], Magdalena Kostrzewska[3], Katarzyna Leszczyńska[2], Ewa Gulczyńska[1]

SUBGALEAL HEMATOMA AS A PERINATAL PRESENTATION OF RARE HEMATOLOGIC PROBLEMS IN NEWBORNS. OWN EXPERIENCE

KRWIAK PODCZEPCOWY JAKO OKOŁOPORODOWA MANIFESTACJA RZADKICH PROBLEMÓW HEMATOLOGICZNYCH U NOWORODKÓW. DOŚWIADCZENIA WŁASNE

[1]Clinic of Neonatology, Polish Mother Memorial Hospital, Research Institute, Lodz, Poland
[2]Department of Radiology, Polish Mother Memorial Hospital, Research Institute, Lodz, Poland
[3]Department of Paediatrics, Oncology, Hematology and Diabetology Medical University of Lodz, Poland

Abstract

***Introduction*:** *Bleeding to the subgaleal space is a rare and often serious complication of childbirth. Delivery with the use of vacuum or forceps is considered as the main risk factor of subgaleal hemorrhage. Reports of other possible causes (including fetal ones) appear rarely.*

Objectives: *The aim of this study is to present and analyze two unusual cases of bleeding to subgaleal space in neonates delivered through caesarean section, in whom two different concomitant hematologic problems were diagnosed. The authors demonstrate also the mechanisms leading to the formation of subgaleal hematoma as well as discuss the impact of the final diagnosis on the course of the perinatal period and the need to modify medical practice in a variety of clinical situations in both newborns and their mothers.*

Material and methods: *Authors present two consecutive cases of severe subgaleal hemorrhage.*

Results: *In the first newborn hemophilia was finally diagnosed. The second neonate was diagnosed with neonatal alloimmune thrombocytopenia.*

Conclusions: *Subgaleal hemorrhage is a rare complication of delivery. In severe cases, other possible risks should be considered apart from the traumatic delivery only. An early identification of potential hematological risk factors can influence the effectiveness of the treatment and help to modify the follow-up of both the infant and its mother.*

Key words: hemorrhage, neonatal alloimmune thrombocytopenia, hemophilia, newborn

Streszczenie

Wstęp: *Krwawienie do przestrzeni podczepcowej stanowi rzadkie, często groźne powikłanie porodu. Jako główny czynnik ryzyka wystąpienia krwiaka podczepcowego wymieniany jest poród z użyciem próżniociągu lub kleszczy. Doniesienia o innych możliwych przyczynach, w tym płodowych są rzadko spotykane.*

Cel: *Celem pracy jest przedstawienie i analiza dwóch nietypowych przypadków wystąpienia masywnego krwawienia do przestrzeni podczepcowej u noworodków urodzonych drogą cięcia cesarskiego, u których rozpoznano współistnienie dwóch różnych problemów hematologicznych. Przedstawiono także mechanizmy prowadzące do powstawania krwiaka podczepcowego, a w dyskusji omówiono wpływ ostatecznie postawionych rozpoznań na przebieg okresu okołoporodowego i konieczność modyfikacji postępowania lekarskiego w różnych sytuacjach klinicznych u obu noworodków i ich matek.*

Materiał i metody: *Omówiono dwa kolejno po sobie występujące w krótkim okresie czasu przypadki rozpoznania krwiaka podczepcowego o ciężkim przebiegu klinicznym.*

Wyniki: *U pierwszego noworodka ostatecznie rozpoznano hemofilię.W drugim przypadku stwierdzono noworodkową alloimmunologiczną małopłytkowość.*
Wnioski: *Krwiak podczepcowy jest rzadkim powikłaniem porodu. W przypadkach o ciężkim przebiegu, należy również rozważyć inne, poza traumatycznym porodem, możliwe czynniki ryzyka jego wystąpienia. Wczesne rozpoznanie ewentualnych hematologicznych czynników ryzyka ma wpływ na skuteczność leczenia i dalsze postępowanie z noworodkiem i jego matką.*

Słowa kluczowe: krwotok, alloimmunologiczna małopłytkowość noworodków, hemofilia / noworodek

DEV PERIOD MED. 2015;XIX,3,I:277-282

INTRODUCTION

The galea aponeurotica or epicranial aponeurosis (*L. aponeurosis epicranialis*) is a tendinous structure which joins two bellies, the frontal and the occipital one, of the occipito-frontalis muscle. In some people this structure is also bilaterally linked with the mutably appearing temporoparietalis muscle (a part of the superior auricular muscle). Both mentioned muscles together with the galea aponeurotica form an anatomical structure called the epicranial muscle. It is closely attached to the skin of the head but only loosely attached to the side of the periosteum (exterior lamella) of the cranium (apart from the place of connection). In the cancellous part of the cranium diploic veins are located. They are connected with the sinuses of the dura mater by the emissary veins (from the internal side) and the extracranial veins, including also the veins draining the epicranilis muscle (from the external side) [1]. An injury of the emissary veins causes bleeding to the subgaleal space and is considered a cause of the formation of the subgaleal hematoma (SH) [2]. In a newborn this space can contain even 260 ml, which is almost all blood of a newborn (80-90 ml/kg). It explains therefore why bleeding to this space is perceived as particularly dangerous and why it can lead to death in 25% of cases [2].

Subgaleal hematoma (SH) appears rarely as a complication of the delivery (0.4-6 cases per 1000 labours). According to the literature, most of SH diagnoses are results of traumatic labour (vaccum or forceps labour) [3]. Other risk factors, such as the lack of cooperation with the mother, a prolonged second period of labour, cephalopelvic disproportion or fetal macrosomia, are rarely listed. Sporadically, the prolonged bleeding to the epricranial structure is reported to be caused by hemostatic disturbance of the newborn [2, 4, 5].

The dynamics of the clinical manifestation may vary due to the venous character of the damaged vessels. Insidious onset of SH may result in a delayed diagnosis and treatment. Commonly observed perinatal traumas, such as cephalohematoma or massive caput succedaneum, can only be the beginning symptoms. The growth in a head circumference is observed during the examination.

A doughy hematoma in palpation is perceived as massive edema. Depending on the volume of the extravasation, blood can be localized in the bottom parts of the head according to gravitation. In an extreme case bleeding can involve all scalp, descending to the neck and forehead (petechiae of the nuchal, eyelids and orbital area can be observed). The layer of the accumulated blood can reach a few centimeters. General symptoms, which are the effect of a massive blood loss, occur simultaneously and include tachycardia and hypotension. Finally a hypovolemic shock develops with following coagulation disturbances. An accurate and fast diagnosis as well as an appropriate treatment is important for successful treatment [3, 7].

THE AIM

The aim of this report is to present two subsequent (occurring in the same calendar year) cases of a subgaleal hematoma as a result of serious perinatal complication. The analysis of clinical course and additional results leading to final diagnosis was performed. The discussion includes the description of the impact of diagnosed hematological disorder on perinatal and neonatal time, as well as follow-up of the babies and account of the situation of their families. We would like to put emphasis on the fact that in the case of following pregnancies of the mothers of both newborns, a modification of obstetric proceeding should be applied.

MATERIALS

Patient 1

A baby boy from the first pregnancy was born in the 39th week of gestation age by caesarean section. The newborn's body mass was 3560 g. The indication for the cesarean section was prolonged labour (attempt of vaginal delivery lasted 20 hours). The newborn was born in a good condition (9 points in the Apgar score in 1' and 5' minute of life). In the physical examination caput succedaneum and suspicion of small cephalohematoma above the left parietal region were found. In the obstetric anamnesis the mother was treated with thyroxin because of the hypothyreosis during pregnancy. The newborn was in a good state and was admitted to the Newborn Department. In the succeeding examination of the baby (8 hours after delivery) cephalohematoma above the left parietalis bone was found (dimension 4 cm). At the end of the first day of life (21 hours since delivery) the massive

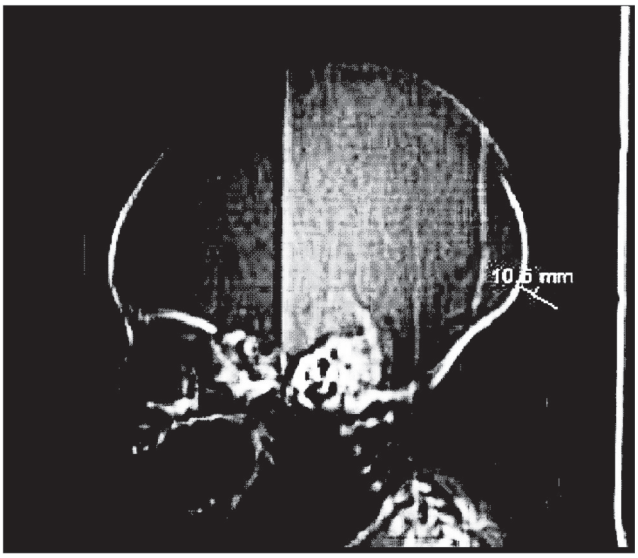

Fig. 1. Panoramic CT scan of the patient No.1.
Ryc. 1. Przeglądowy skan CT pacjenta nr. 1.

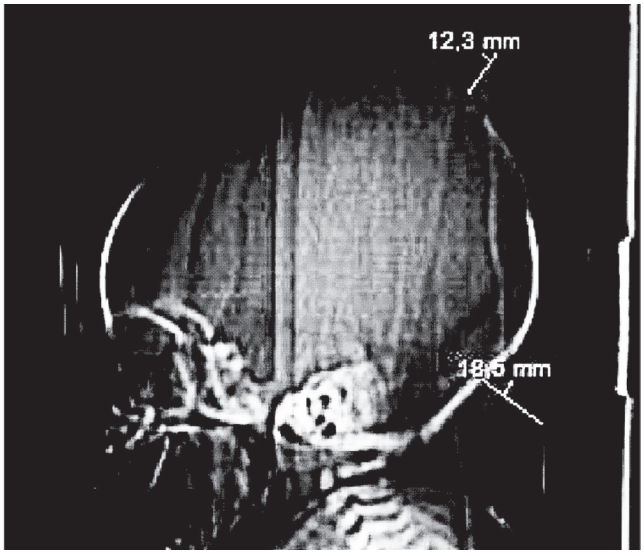

Fig. 2. Panoramic CT scan of the patient No. 2.
Ryc. 2. Przeglądowy skan CT pacjenta nr 2.

edema of the head was observed. The head circumference increased from 35 to 39 cm. The baby presented pallor of the skin, bruising and petechie in the orbital area and the neck. Laboratory test revealed severe anemization (Htk 15.1%, Hb 5.4 g/dl), the white blood cells and platelet concentration were in normal range (WBC 15.36 k/µl, PLT 188 k/µl). Immediately leukoreduced, irradiated packed red blood cells were transfused (PRBC-LR-IR). In the head sonography subgaleal hematoma was described and a suggestion of the bleeding to the subarachnoid space was made. Computer tomography confirmed the presence of the massive subgaleal hematoma and a small amount of blood in the subarachnoid space (fig. 1). There were no indications for the neurosurgical intervention. In the laboratory tests progressive hypocoagulability and thrombocytopenia were observed (tab. I). The material for the identification blood clot factors was secured. An attempt to rebalance the hemostasis instability by plasma and platelets transfusion was performed without any success. The level of the AT III was rebalanced with antithrombin III. It should be noted that the levels of VIII factor were particularly low (tab. II). The suspicion of the hemophilia A was made. The treatment with recombinant factor VIII (Advate, 50 U/kg every 8 hours) was started immediately after hematological consultation. This treatment normalized coagulation and blood parameters. In the sixth day of life the patient in the good state, cardiologically and respiratorily stable, was transferred to the Hematology Department of the Pediatric in Medical University Institute in Łódź, where the definite diagnosis of a severe form of hemophilia A was made.

Patient 2

A baby boy from the first pregnancy was born in the 41st week of gestation age by caesarean section. The birth body mass was 4020 g. The indication for the caesarean section was obstructed labour (the labour started spontaneously, caesarean section was performed after 2 hours of labour duration). In the obstetric anamnesis during the pregnancy polihydramion was observed. The mother received ampicillin before delivery because of positive GBS (Sreptococcus agalactiae) screening test. Her C-reactive protein (CRP) level was increased. After the delivery, the state of the newborn was good, with 9/9 point in the Apgar score. In the physical examination a massive caput succadeum and petechie on the head and back were described. In the second hour of life the edema of the head increased and the first suggestion of the subagaleal hematoma was made. The presence of the new petechie and the progression of the first one were observed on the whole skin of the newborn. The baby, cardiologically and respiratorily stable, was transferred to the Clinic of Neonatology. Because of the perinatal history, the inborn infection with massive disturbances of coagulology was suspected. The samples for the bacteriological culture (blood, secretion from stomach, smear from the skin) were taken before the antibiotic therapy was started. In the laboratory test severe thrombocytopenia (PLT 24 k/ul) without any significant disturbances in coagulation parameters was found (tab. I). The assessment of the blood clotting factors activity did not show any important abnormalities (tab. II). The urgent sonography and computer tomography confirmed the subgaleal hematoma. Due to the progression of anemization (caused by bleeding to the epicranial structure), platelets and blood (RBC-LR-IR) were transfused. The transient improvement of the platelets level was obtained, but in the 5th day of life the next platelet transfusion was necessary due to the progression of the thrombocytopenia. After the verification of bacteriological tests and the normalization of the CRP level, the suggestion of immune thrombocytopenia was made. The intravenous immunoglobulin was provided and the stabilization of the platelets level was achieved. The analysis from the Institute of Hematology and Transfusiology in Warsaw confirmed neonatal alloimmune thrombocytopenia (NAIT). In the mother's plasma antibodies anty-HPA-

Table I. Coagulation results from the first day of life of both patients (before treatment).
Tabela I. Wyniki koagulogramu z pierwszej doby życia obu pacjentów (przed leczeniem).

Parameter ***Parametr***	**Unit** ***Jednostka***	**Patient 1** ***Pacjent 1***	**Patient 2** ***Pacjent 2***
PT Prothrombin time *Czas protrombinowy*	[s]	16.3	14.8
Prothrombin index *Wskaźnik protrombinowy*	[%]	60	74
International Normalized Ratio INR	-	1.7	1.4
Activated Partial Thromboplastin Time APTT	[s]	lack of clot *brak skrzepu*	26
TT Thrombin time *Czas trombinowy*	[s]	22.7	20.5
Fibrinogen *Fibrynogen*	g/L	1.28	1.53
Platelet *Płytki krwi*	$1x10^3$/uL	111	24

Table II. Activity of the coagulation factors from the first day of life for both patients (before treatment).
Tabela II. Wyniki aktywności czynników krzepnięcia z pierwszej doby życia u obojga pacjentów (przed leczeniem).

Clot factor ***Czynnik krzepnięcia***	**Unit** ***Jednostka***	**Patient 1** ***Pacjent 1***	**Patient 2** ***Pacjent 2***
II	%	31.4	46.9
V	%	34.4	94.5
VII	%	14.9	43.4
VIII	%	0.6	251
IX	%	28.9	41.1
X	%	34.5	38.6
XI	%	21.5	54.1
XII	%	26.5	55.5
XIII	%	23.2	58.5
Wv	%	255.4	286

3b were observed. The molecular test has revealed the presence of HPA 3b antigen on the baby's and his father's platelets. Finally, in the 18th day of hospitalization, the newborn was discharged home in a stable condition. The ambulatory hematological care was recommended for the mother and the child.

DISCUSSION

Both reported cases occurred in the short period of time and were the only cases of the severe and demanding multidirectional treatment of subgaleal hematoma in the same calendar year. (There are about 5000 deliveries each year in the Polish Mother Memorial Hospital). Both babies have been delivered by c.s., so the main risk factors of the SH (forceps and vacuum delivery) were not present. It should be stressed however that in these cases the additional risk factors (the unsuccessful attempt at the natural labour and fetal dystocia) existed.

The presented patients differed in the dynamic of the progression of the subgaleal hematoma. In the first patient the diagnosis was made after 20 hours of life, whereas in the second one after 2 hours. The rapid progression of the heamatoma is a characteristic complication after vacuum labour (often the symptoms of SH are presented in the first minute after delivery) [3, 4]. The differences in the dynamics and the intensity of the symptoms can be explained with a different size of the injured blood vessel

or with a different kind of damage in hemostasis system [3]. In the presented cases the variation on progress was probably connected with a different mechanism leading to the instability of hemostasis. In the first patient the coagulation cascade was disturbed and in the second one the creation of the platelet plug was impaired. The vasospasm and the creation of the platelet plug are the first responses to bleeding (primary hemostasis), while coagulation with the coagulation factors stabilize the process and lead to the healing of the vessel injury (secondary hemostasis) [8, 9].

In the first case, securing the plasma sample for coagulation and the factors assay before the fresh frozen plasma transfusion, led to the prompt diagnosis of the hemophilia A and enabled starting the appropriate and effective treatment. In the parental family history there were no cases of hemophilia. According to the literature, around 30 % of the hemophilia cases result from a spontaneous mutation [10]. It is worth noting that the mother has only female siblings (3 sisters). In light of reports in the literature, only 30-60 % of severe forms of hemophilia are recognized in the neonatal period [11, 12, 13]. The presented case is an example of a prompt diagnostic process of the severe hemophilia A caused by extreme factor VIII insufficiency. The early substitution of recombinant factor VIII normalized the parameters of the hemostasis and protected the patient from further complications. On the one hand, an early diagnosis of hemophilia mostly gives evidence of the severe form of the disease, but, on the other hand, an early treatment can help ease the long-term complications of the condition.

In view of the the possible procreation plans of the mother and her sisters and the fact that the women could carry the mutation, the family should be taken care of by the genetic outpatient clinic. In that case preimplantation and postconceptive diagnosis is possible. Regardless of a baby's genotype, mothers who are hemophilia carriers should be referred to the tertiary referral health clinic, experienced in the treatment of pregnant women with coagulopathy. In the case of diagnosis of hemophilia in the fetus there is no preference for caesarean section over natural delivery. However, in the situation of a prolonged labour, or other complications, in order to avoid vacuum or forceps, a quick decision to perform the cesarean section should be taken [14, 15]. It is strictly forbidden to take blood samples from the fetus scalp, or to perform any other action (including the intramuscular vitamin K administration), as they can lead to bleeding [16].

Neonatal alloimmune thrombocytopenia (NAIT) can appear in the first pregnancy (even 50% of cases of the NAIT) [17]. According to the literature, NAIT is present in 1/600 to 1/8000 pregnancies. Because of the mild and transient course of the neonatal thrombocytopenia, the incidence of NAIT is probably underestimated [18, 19]. One of the most severe complications of NAIT is intracranial hemorrhage (ICH), which is diagnosed (often prenatally) in 10-25% of cases. In view of this fact every newborn with thrombocytopenia should be examined with ultrasonography of the head (including mastoid fontanel window) [18]. In the presented patient, in spite of massive symptoms connected with disturbances in hemostasis, the bleeding to the central nervous system did not occur. The appropriate treatment allowed for the normalization of the platelets level and the patient's condition improved. The primarily suspected infection was hence verified and excluded. However, it is important to remember that in the case of congenital thrombocytopenia both these causes can exist. The suspicion of the infection (including CMV and fungal infections) should be excluded. In the cases resistant to the treatment, neonatal alloimmune thrombocytopenia should be considered. According to the data from 2014 (data review of 59425 newborns), NAIT is the cause of 27% of cases of severe congenital thrombocytopenia [18]. The treatment of NAIT should decrease the risk of severe neurological complications (ICH), so the safe platelets level should be obtained (above 30 k/μl in a stable full-term newborn). In urgent situations, random donor platelets could be administered, but specific (NAIT inducing) antigen negative platelets give a better treatment effect in platelet increment and a longer half-life of transfused platelets. A diagnosis (serological and genotyping) and a further preparation of antigen negative platelets is time consuming, so random donor platelet are often the first line of treatment option. A mother could be a donor of antigen negative platelets (mother's platelets do not have antigens against the alloantibodies) [20]. Despite the obvious availability of the mother, this "source" of platelets is rarely used in the treatment of NAIT. The problem with this approach derives from the mother's eligibility to be a donor as well as from the fact that the process of plasma reduction (which is obligatory in this case) affects platelets recovery and function [21]. Intravascular immunoglobulin is easily available and proved to be effective in the treatment of NAIT. Because of the time needed to achieve an increase in platelets count, this option is used as parallel to platelets transfusion. In the milder forms of NAIT (without severe thrombocytopenia and features of bleeding diathesis) the use of immunoglobulin may be the only way of treatment [17, 22]. A total diagnosis, together with the genotyping of the baby's and the father's platelets antigens, gives important information needed for planning the subsequent pregnancies. A pregnant woman, with NAIT diagnosed in a previous baby, should be referred to the tertiary obstetric clinic, which specializes in the treatment of women with hematologic problems. She should also stay under the constant care of a hematologist. The information about the mother's alloantibodies and genotyping of the father's platelet antigens provide information about the risk of NAIT in a fetus. It is possible (from the mother's blood or amniotic fluid) to determine the genotype of fetal platelets antigens as early as in the 18th week of gestation. This could confirm or exclude NAIT in the current pregnancy. An appropriate treatment in the pregnancy with NAIT is still debatable. Early immunoglobulin infusion as well as prednisone administration gives encouraging results. Sometimes, especially in the case of high-risk pregnancies (with a history of previous intracranial bleeding), the repeated intrauterine (antigen negative or random donor) irradiated platelets transfusion could be recommended [21, 23].

CONCLUSIONS

1. Subgaleal hematoma is a rare complication of the childbirth. It can be a manifestation of the various mother and fetal hematological problems.
2. An appropriate treatment reduces the risk of the potential complications connected with massive bleeding to the subgaleal space.
3. A rapid diagnosis including rare hematological disorders allows for the implementation of an effective treatment.
4. Giving the full diagnosis has a great impact on the therapeutic process of the newborn. It is also important for the preparation for the next pregnancies (for assessing their potential risks) and for the correct monitoring of a mother in pregnancy by the obstetrics (in the cooperation with a hematologist).

REFERENCES

1. Sinelnikov RD. Atlas Of Human Anatomy Tom I, Mir Publishers, ISBN 5-03-000322-3, Moskwa, 1988;286.
2. Wetzel EA, Kingma PS. Subgaleal hemorrhage in neonate with factor X defitiency following a non-traumatic cesarean section. J Perinatol. 2012;32:305-305.
3. Thorup L, Koch KU. Neonatal subgaleal haemorrhage causing fatal course after vacuum-assisted extraction. Ugeskr Laeger. 2013;7(175):34-35.
4. Nasseri F, Badiei Z. Neonatal subgaleal hemorrhage „a fatal complication of vacuum extraction delivery". Iran J Ped. 2007;17:297-301.
5. Kilani RA, Wetmore J. Neonatal subgaleal hematoma: presentation and outcome-radiological findings and factors associated with mortality. Am J Perinatol. 2006 Jan;23(1):41-48.
6. Davis DJ. Neonatal subgaleal hemorrhage: diagnosis and management. JAMC, 2001;164:1452-1453.
7. Parker LA. Part 1: early recognition and treatment of birth trauma: injuries to head and face. Adv Neonatal Care. 2005;5(6):288-297.
8. Clemetson KJ. Platelets And Primary Haemostasis. Thrombosis Research. 2012:129(3):220-224.
9. Haley KM, Recht M, McCarty OJ. Neonatal platelets: mediators of primary hemostasis in the developing hemostatic system. Pediatr Res. 2014;76(3):230-237.
10. Chalmers EA. Neonatal coagulation problems. Arch Dis Child Fetal Neonatal Ed 2004;89:475-478.
11. Pollman H, Richter H, Ringkamp H. Jurgens H. When are children diagnosed as having severe haemophilia and do they start to bleed? A 10-year single-centre PUP study. Eur J Pediatrics. 1999;158:166-170.
12. Kulkarni R. Perinatal management of newborns with haemophilia. Br J Haematology 2001;112:264-274.
13. Conway JH, Hilgartner MW. Initial presentations of pediatric hemophiliacs. Arch Ped Adoloscent Med 1994;148:589-594.
14. Walker ID, Walker JJ, Colvin BT, Letsky EA, Rivers R, Stevens R. Investigation and management of haemorrhagic disorders in pregnancy. J Clin Pathol. 1994;47:100-108.
15. Ljung R, Lindgren AC, Petrini P, Tengborn L. Normal vaginal delivery is to be recommended for haemohilia carrier gravidae. Acta Paediatrica. 1994;83:609-611.
16. Dyson H. Neonatal haemophilia-a guide to recognition and management. Infant. 2006;2(4):156-159.
17. Roback JD, et al. Technical manual (16th ed.). 2008, Bethesda, Md. American Association of Blood Banks, ISBN 1563952602.
18. Kamphuis MM, Paridaans N, Porcelijn L, De Haas M, Van Der Schoot CE, Brand A, Bonsel GJ, Oepkes D. Screening in pregnancy for fetal or neonatal alloimmune thrombocytopenia: systematic review. BJOG. 2010;117(11):1335-1343.
19. McFarland JG, Aster RH, Bussel JB, Gianopoulos JG, Derbes RS, Newman PJ. Prenatal diagnosis of neonatal alloimmune thrombocytopenia using allele-specific oligonucleotide probes. Blood 1991;78 (9):2276-2282.
20. Dębska M. Feto-maternal alloimmune thrombocytopenia. Post N Med. 2009;8:628-634.
21. Mcquilten ZK, Wood EM, Savoia H, Cole S. A review of pathophysiology and current treatment for neonatal alloimmune thrombocytopenia (NAIT) and introducing the Australian NAIT registry. Aust N Z J Obstet Gynaecol. 2011;51(3):191-198.
22. Bakchout T, Bassler D, Heckmann M, Thiele T, Kiefel V, Gross I, Arnold DM, DiTomasso J, Smith JW, Paes B, Greinacher A. Management of infant born with severe neonatal alloimmune thrombocytopenia: the role of platelet transfusions and intravenous immunoglobulin. Transfusion 2014;54(3):640-645.
23. Espinoza JP, Caradeux J, Norwitz ER, Illanes SE. Fetal and Neonatal Alloimmune Thrombocytopenia. Rev Obstet Gynecol. 2013;6(1):e15-e21.

Author's contributions/Wkład Autorów
According to the order of the Authorship/Według kolejności

Conflicts of interest/Konflikt interesu
The Authors declare no conflict of interest.
Autorzy pracy nie zgłaszają konfliktu interesów.

Received/Nadesłano: 27.01.2015 r.
Accepted/Zaakceptowano: 26.05.2015 r.

Published online/Dostępne online

Address for correspondence:
Tomasz Talar
Clinic of Neonatology, Polish Mother Memorial Hospital, Research Institute, Łódź, Poland
281/289 Rzgowska Street, Lodz
tel. (42) 271-10-41/53
fax. (42) 271-10-40
tel. 501-617-820
e-mail: tomtal@wp.pl