

CASE STUDY

A CLINICAL CASE OF ARTERIAL THROMBOSIS IN A PREMATURE BOY WITH NEONATAL SEPSIS AND HIGH RECTAL ATRESIA

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ABSTRACT

Occlusion of the venous or arterial vessels in childhood is rather rare but dangerous complication. Occurrence of neonatal thrombosis is 0.5 per 10 000 of live newborns. Promoting factors include congenital defects of coagulation, maternal diabetes, neonatal sepsis, necrotic enterocolitis, asphyxia, and metabolic diseases. More than 90 % cases of neonatal thrombosis are associated with catheterization (umbilical arterial or venous, other central venous lines). Acute arterial thrombosis caused by a peripheral venous catheter is very rare complication, but it can result in severe consequences.

The article contains a clinical case of right brachial artery thrombosis in a premature boy with extremely low body weight complicated by development of dry gangrene and amputation of the limb. Complex risk factors promoting development of neonatal arterial thrombosis were found: preterm birth, neonatal sepsis, possible incorrect insertion of a peripheral venous catheter. Associative factors were congenital developmental defects of the intestine (high rectal atresia) and heart (bicuspid aortal valve, open oval foramen), and maternal factors. The authors emphasize their attention on the necessity to continuous education of the medical staff concerning the technique of catheter insertion and care of them, absolute implementation of safety policy concerning nosocomial infection, adequate provision of ultrasound examination devices with high rarefaction sensors, involvement of a multi-disciplinary team of specialists to manage complicated clinical cases.

KEY WORDS: thrombosis; amputation; premature infant; neonatal sepsis; anal atresia

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INTRODUCTION

Babies born before complete 37 weeks of gestation are considered to be premature. The WHO estimates about 15 million of children in the world to be born prematurely. Complications resulting from preterm delivery are the main cause of lethal outcome among children under 5 years. Thus, in 2015 they caused death of about 1 million of children. Three fourths of those deaths could be prevented by means of the existing means, even without an intensive care unit. The index of preterm delivery varies from 5 to 18 % of neonates. Premature babies are divided into categories depending on the terms of gestation: extremely premature (less than 28 weeks); considerably premature (from 28 to 32 weeks); moderately premature (from 32 to 37 weeks) [1].

Occlusion of the venous or arterial vessels in childhood is rather rare but dangerous complication. Occurrence of neonatal thrombosis is 0,5 per 10 000 of live newborns. Promoting factors include congenital defects of coagulation, maternal diabetes, neonatal sepsis, necrotic enterocolitis, asphyxia, and metabolic diseases. Though, more than 90 % cases of neonatal thrombosis are associated with catheterization (umbilical arterial or venous, other central venous lines). Acute arterial thrombosis is an extremely rare complication caused by a peripheral venous catheter. Its treatment requires involvement of a multi-disciplinary team of specialists [2-4]. Tsonis O. et al. (2020) indicate that neonatal arterial thrombosis can occur even during

delivery; and cases with a low risk with the lack of visual promoting factors can be of a great danger for limb-sparing, in case appropriate measures are not initiated [5].

The main goal of this article is the presentation of clinical case of arterial thrombosis in a premature boy with neonatal sepsis and high rectal atresia.

Informed written consent about publication of case report and pictures was obtained from parents. This study was conducted in compliance with the basic provisions of the Good Clinical Practice (1996), Council of Europe Convention on Human Rights and Biomedicine (1997), Helsinki Declaration of the World Medical Association on Ethical Principles for Medical Research (1964 - 2008).

CASE REPORT

The boy's body weight at birth was 900 g, the body length 34 cm. The boy was born to X pregnancy (I degree anemia, vegetative-vascular dystonia, varicose veins of the lower limbs, respiratory infection at 20 weeks of gestation), X delivery in 29 weeks of gestation by means of caesarian section due to premature abruption of the normal placenta, and uterine bleeding. Waterless period was 15 days and 5 hours. The mother received antenatal prevention of respiratory distress-syndrome for her baby (24 mg of Dexamethasone). USD conducted at 29 weeks of gestation found low weight for the gestational term, the signs of

cardiomyopathy, hydropericardium, inconsiderable aortal stenosis and extreme oligo(hydr)amnios; there was no pathology found from the site of the digestive tract and urinary system.

Findings of the obstetrical anamnesis: I-IV pregnancy – mature babies with the body weight more than 3000 g, V pregnancy – mature baby with the body weight of 2480 g (antenatal death), VI pregnancy – 35 weeks of gestation with the body weight of 2500 g, VII pregnancy – 35 weeks of gestation with the body weight of 2500 g, VIII pregnancy – 34 weeks of gestation with the body weight of 2000 g, IX pregnancy – 34 weeks of gestation with the body weight of 2130 g.

The baby's condition at birth was assessed as severe at the expense of severe respiratory disorders, pronounced inhibition syndrome with low body weight and prematurity. Primary examination found the signs of congenital developmental defects of the intestine – anal atresia. The 1 minute Apgar score was 4 (2-1-0-0-1), the 5 minute score was 6 (2-1-1-1-1), the 10 minute score was 6 (2-1-1-1-1). A complex of resuscitation measures was initiated: lung inflation followed by tracheal intubation and mechanical ventilation through the intratracheal tube with 30 % oxygen, catheterization of the umbilical vein and injection of warm 0,9% NaCl solution 10 mg/kg. After the baby's condition was stabilized, natural pulmonary surfactant Poractant alfa in the dose of 200 mg/kg phospholipids was introduced by means of an invasive method.

The baby's condition remained extremely severe during the first day of life due to III degree respiratory failure, signs of hypoxic-ischemic damage of the nervous system and congenital developmental defect – anal atresia. Neurologically pronounced inhibition syndrome was detected. The skin and visible mucous membranes were rose-pink and warm by touch. Mechanical ventilation was conducted from both sides, rales were absent. Heart sounds were sonorous and rhythmical; HR was 120 beats per minute. Arterial BP corresponded to the gestational term. The tongue was moist and not coated. The abdomen was enlarged in the volume, bloated, symmetrical, participates in respiration by all the portions regularly, palpatory soft but tender. Symptoms of the peritoneal irritation were negative, peristalsis was intensified. Spontaneous and stimulated defecation was absent, urine with meconium admixtures. The baby was taken care of at the III level intensive care unit, in the infant incubator, under protective regimen. Traditional mechanical ventilation was carried out in the regimen of normal ventilation with FiO₂ 0.21. The baby received parenteral nutrition, empiric antibiotic therapy (penicillins and aminoglycosides in appropriate age doses) and anaesthetic therapy through the umbilical vein by means of an umbilical catheter. Continuous stomach decompression was performed through the orogastric probe. Results of laboratory findings were within physiological limits.

Provisional diagnosis: congenital developmental defect of the intestine: anal atresia. Low intestinal permeability. Primary lung atelectasis. III degree respiratory failure. 29 weeks prematurity.

On the 1st day of life the baby was transferred to the surgical department of the children hospital, IV (specialized) level. According to clinical data and results of Wangenstein X-ray examination the surgical diagnosis was made: high rectal atresia with abscess into the urethra or urinary bladder. The pathology required immediate surgery after the baby's condition was stabilized, and starting adequate preoperative preparation.

On the 2nd day of life surgery was performed keeping to the rules of surgical asepsis in the resuscitation room under conditions of the infant incubator and appropriate thermal conditions. The surgery consisted of left lateral laparotomy; separate sigmoid stoma was delivered (distal and proximal portions of the sigmoid colon were delivered as stomas).

The stoma started functioning on the 3rd day after surgery, but general baby's condition remained severe due to manifestation of the syndrome of multiple organ failure. In the dynamics of disease the child developed signs of severe respiratory failure and cardiovascular failure, which required invasive ventilation support and indication of inotropic support.

On the 10th day of life the patient manifested signs of late neonatal sepsis associated with considerable increase of pro-inflammatory markers in the blood (leukocytosis higher 30*10⁹/L, neutrophil index more than 0.7, C-reactive protein more than 24 mg/L). Due to possible neonatal infection antibiotic therapy was corrected with step-by-step change of the combination of III generation cephalosporin and aminoglycoside, carbapenem and aminoglycoside, to fluoroquinolone monotherapy. The total duration of antibiotic therapy lasted 28 days. Echocardiography determined the signs of congenital heart defect – bicuspid aortal cusp and open oval foramen (d = 5.1 mm).

It should be noted that umbilical catheter was removed on second day of life, during admission to the surgical department. Attempts to find the central vein (subclavian, jugular or femoral) to give infusions by means of the technical means available failed. Catheters were inserted into the right ulnar vein and dorsal vein of the left foot. Then repeated venipunctures were made due to the lack of function of the peripheral veins punctured before.

On the 12th day of life venipuncture was made in the right cubital fossa (catheter 24G Abbocatch) for continuous infusions. On the 13th day of life the right upper limb was noticed to become cyanotic and grey to the ulnar bend, nail bones of the right hand became black, but local skin temperature and pulsation of the major vessels remained normal. The catheter was immediately removed from the peripheral vein. On the 14th day of life cyanosis of the right upper limb spread to the upper third of the right upper arm.

First cyanosis and swelling of the right hand was observed with retained movements in the fingers and hand. Then against the ground of the above symptoms the nail bone of the II right finger was detected. On the 16th day of life nail bones of I-V finger of the right hand became black, and the skin became cyanotic and grey. It spread to the upper third of the right upper arm, and pulsation of the arteries was not detected. On the 17th day of life the

hand and forearm became black, vascular pulsation in the portion of the middle third of the upper arm was not found, though it was felt on the level of the axillary artery. Dry gangrene of the right upper arm was diagnosed. On the 19th day of life the right upper limb till the level of the upper third of the upper arm is cold and dry by touch, black in color, insensitive; movements are possible due to mobile shoulder joint, bending of the hand and elbow joint is possible, but unbending is not, unclear demarcation line is determined (Fig. 1). Due to impossibility to restore blood supply in the limb, amputation was performed on the level of the upper third of the right upper arm.

It should be noted that the child presented the signs of marked hypocoagulation with underling neonatal sepsis, which prevented from the possibility to initiate anticoagulation and/or fibrinolytic therapy with the aim to achieve conservative thrombolysis.

Nineteenth day of life. Progress of surgery. The surgery was performed in the resuscitation room under conditions of the infant incubator and appropriate thermal conditions. The baby was in the supine position, the upper part of the trunk was on the roller, and the upper arm was moved to the border of the infant incubator. First, the anterior-external flap was cut by means of semi-oval incision in order to retain *m. deltoideus*, playing an important role for the movements of the stump.

1. The cut was made along sulcus deltoideopectoralis from the clavicle to the inferior border of the greater pectoral muscle (*musculus pectoralis major*). The latter was cut transversally not far from the point of attachment to the humeral bone. розікали поперек, недалеко від місця прикріплення до плечової кістки. The sheath of *m. Coracobrachialis* was opened, the muscle was drawn laterally; after the posterior wall of the sheath was opened *a. and v. axillaris* were secured.

2. The skin surrounding *m. deltoideus* anteriorly, inferiorly and posteriorly was cut. The muscle was cut out from the point of attachment to the humeral bone and drawn upward together with the skin. Special attention was paid to retaining *n. axillaris*, innervating the muscle.

3. The tendons of *m. latissimi dorsi* and *m. teretis majoris* were cut. After that a transverse cut was made on the level of the upper margin of the posterior incision of the skin surrounding the upper arm from the inside.

4. The soft tissues were cut till the bone. The soft tissues were drawn maximum upwards. The periosteum was cut moving it downward, and the humeral bone was sawn (Fig.2, Fig. 3).

5. Hemostasis was performed by means of electric coagulator. The nerve trunks were isolated and cut. Sutures were applied on the muscles and skin.

Considering high growth intensity of the humeral bone at the expense of the proximal germ cartilage, the cut-off part of the humeral bone was covered with a considerable amount of the soft tissues. Due to considerable contractile ability of the skin in children, the cut along the anterior surface was made 3 cm distally than that along the posterior surface.

The following principles were kept to while performing amputation: a) supply the stump with sufficient amount of the soft tissues; b) Fig. retention of every centimeter of the limb due to the lag of growth of the diaphysis stump as compared with the appropriate segment of a healthy limb (Fig. 4).

As a number of authors admit, arterial thromboembolism with a venous catheter is a rare complication [2-5]. Considering literature data, experience of the home and foreign specialists, as well as peculiarities of the given clinical case, we can suggest several causes promoting development of the complication.

One of the probable causes of arterial thrombosis of the newborn boy with an extremely low body weight were multiple punctures of the peripheral cubital vein and iatrogenic damage of the arterial branch located close, followed by thrombosis of the brachial artery and development of dry gangrene of the limb. Berzel S. et al. (2014) consider that similar situation can occur even without violation of the technique to insert a peripheral venous catheter, as it can be caused by traumatization of the adjacent artery due to the movements of the elbow joint without its artificial stabilization [2]. Complications can occur in case of direct puncture of the brachial or axillary arteries, since causative factors are condition of the vessels of a patient, anatomical peculiarities of the arteries, the point of puncture, success of the first attempt of puncture, and hermetic/sterile bandage [6, 7].

Bacciedoni V. et al. (2016) suggest that factors increasing development of neonatal thrombosis are premature birth and perinatal asphyxia. Premature babies are prone to clot formation due to peculiarities of coagulation system which is characterized by functional immaturity. Premature babies have low activity of antithrombin, and its normal degree of activity is achieved only at the age of 6 months. The children from this group have reduced activity of the fibrinolytic system resulting from decreased plasminogen activity and increased concentration plasminogen activator inhibitor [3]. This suggestion is confirmed by a group of researchers headed by Makatsariya A. (2020), who admit that babies with the gestation age of 22-27 weeks are the biggest risk group concerning development of neonatal thromboembolism [4].

It should be noted that in this particular clinical case, in addition to premature delivery, other provocative factors of neonatal thrombosis cannot be excluded including genetic disorders (congenital developmental defect of the intestine – high rectal atresia with an abscess into the urethra or urinary bladder; congenital heart defect – bicuspid aortal valve, open oval foramen, and prenatal factors which can be indicative of disorders in coagulation processes of the mother (varicose veins of the lower limbs, premature abruption of the normal placenta). The factors presented can be associated with pro-thrombotic gene polymorphism (F5Leiden, F2G220210A, PAI-1 etc). Belousova T.V. et al. (2018) recommend to examine all the children with thrombosis episodes irrespective of their origin concerning carriage of the major markers of thrombophilia and considering issues of the secondary prevention [8].



Fig. 1. The dry gangrene of the right upper arm (19th day of life).

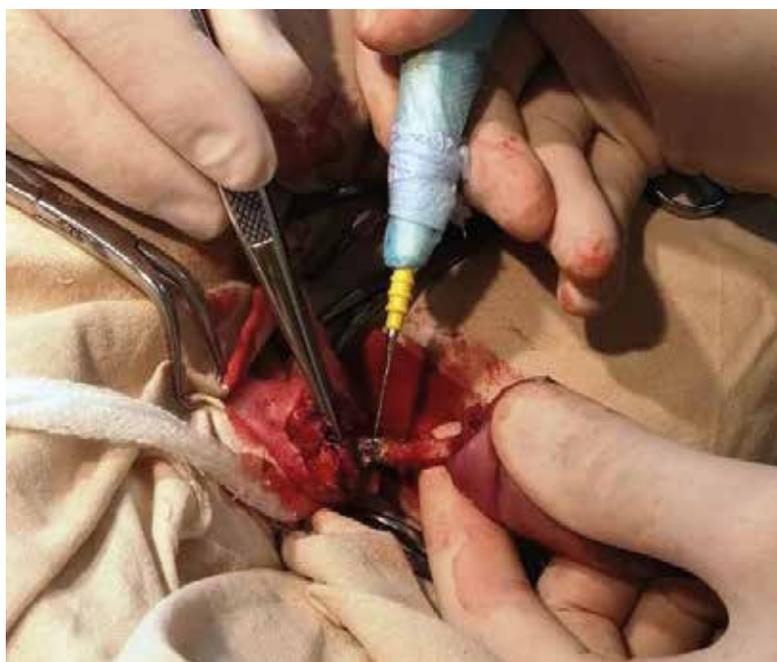


Fig. 2. The dry gangrene of the right upper arm; the stage of amputation; the humeral bone is sawing (19th day of life).



Fig. 3. The dry gangrene of the right upper arm; the right upper limb was amputated (19th day of life).



Fig. 4. The stump of the right upper limb; the stage after surgery (3rd month of life).

To our opinion, one of the possible factors promoting occurrence of thrombosis in this particular case is neonatal sepsis which might be complicated by clot formation in the deep veins of the lower limbs. We can suggest that a clot was isolated in a thrombophlebitic focus not clearly found, and it penetrated into the systemic circulation through the open oval foramen during the right-left bypass, and as a result, into the brachial artery (paradoxical embolism). Thrombus/embolus during its contact with the arterial wall caused a long spasm of the peripheral portion of the blocked artery, pathological changes of the endothelium of the vascular intima and secondary thrombosis spread

along the brachial artery involving the collateral portions. Almuhy R. A. H. (2020) admitted that it is an infectious factor that causes 7,3 % cases of deep venous thrombosis in children [9]. Makatsariya A. et al. (2020) consider septic processes and premature birth as two major trigger factors promoting the risk of neonatal thromboembolism [4].

The necessity to carry out Doppler technique with the use of high rarefaction sensors to control the blood flow along the suspected pathological vessel should be indicated [2, 5]. Berzel S. et al. (2014) presented a case of acute thrombosis of the brachial artery of a newborn caused by a peripheral venous catheter. The authors emphasize that it was timely

Doppler examination of the damaged limb that enabled to diagnose the level of occlusion of the brachial artery and find the signs of early collateralization. The latter fact was a reason to postpone surgery and apply conservative therapy (non-fractional heparin and low molecular weight heparin) [2]. Unfortunately, in our clinical case we were not able to carry out Doppler examination of the patient due to his extremely low body weight and the lack of sensors with appropriate frequency detection.

CONCLUSIONS

Acute arterial thrombosis caused by a peripheral venous catheter is very rare complication, but it can result in severe consequences. The provocative factors during the neonatal period are premature birth, sepsis, violation of the technique to insert catheters, genetic disorders of the hemostasis system etc. We consider that to reduce the frequency of complications after catheterization of the central and peripheral vessels of neonates is possible by means of continuous education of the medical staff concerning the technique of catheter insertion and care of them, absolute implementation of safety policy concerning nosocomial infection, adequate provision of ultrasound examination devices with high rarefaction sensors, involvement of a multi-disciplinary team of specialists (pediatric surgeons, anaesthesiologists, neonatologists, hematologists, sonologists) to manage complicated clinical cases.

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