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Pathogenetic phenotypes of bone cement implantation syndrome in pediatric oncology patients: Case reports

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ABSTRACT

Bone cement implantation syndrome in pediatric oncology patients remains poorly understood. A multimodal pathogenetic model determines the existence of two distinct clinical and pathophysiological phenotypes of this condition: the anaphylactic phenotype (distributive shock) and the embolic phenotype (obstructive shock). Both phenotypes are associated with coagulopathy, with thrombotic catastrophes representing their most severe manifestation. The pathways of thrombotic complications depend on the clinical and pathophysiological phenotype of this critical condition: in anaphylactic bone cement implantation syndrome, they are primarily driven by microthrombogenesis, whereas in embolic bone cement implantation syndrome, both microthrombogenesis and fibrinogenesis contribute to thrombosis. In the first clinical case, bone cement implantation syndrome developed through an anaphylactic mechanism. A boy with femoral osteosarcoma underwent bone cement spacer implantation following tumor resection. We assume that sensitization occurred during this period. This is supported by the presence of a periosteal reaction in the upper third of the right femur, as revealed by computed tomography (CT). During knee endoprosthesis implantation, the patient developed severe hemodynamic instability, cardiac rhythm disturbances, and oxygenation impairment. Despite the characteristic microthrombogenesis mechanism of this pathophysiological phenotype, multiorgan failure and life-threatening thrombotic complications were successfully averted due to effective anti-shock measures and early initiation of heparin therapy. Second clinical case illustrates the embolic phenotype of bone cement implantation syndrome. A boy with tibial osteosarcoma experienced hypotension, tachyarrhythmia, desaturation, and hypocapnia following bone cement application during endoprosthetic surgery. Postoperatively, desaturation persisted. CT revealed a mural defect in the left pulmonary artery and segmental obstructions in multiple branches of both lungs, along with elevated D-dimer levels and echocardiographic evidence of increased right heart pressure. By postoperative day 20, oxygen saturation normalized (the patient was breathing ambient air). CT imaging showed resolution of the filling defect in the left pulmonary artery; however, signs of segmental pulmonary artery obstruction remained in the upper and middle lobes of the right lung and the lower lobe of the left lung. Thus, the hemodynamic catastrophe in the embolic phenotype of bone cement implantation syndrome represents a classic presentation of obstructive shock with subsequent thrombotic complications, driven by the combined mechanisms of microthrombogenesis and fibrinogenesis. The proposed pathogenetic phenotyping of bone cement implantation syndrome allows for a targeted approach to the prevention and treatment of hemodynamic and thrombotic complications in affected patients. This approach appears to be relevant and has the potential to reduce the incidence of adverse outcomes and complications.

Keywords: bone cement implantation syndrome; thrombosis pathogenesis phenotypes; children; intensive therapy; oncology; case reports.

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Патогенетические фенотипы синдрома имплантации костного цемента у детей с онкологическими заболеваниями: клинические наблюдения

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АННОТАЦИЯ

Синдром имплантации костного цемента у детей с онкологической патологией изучен недостаточно хорошо. Мультимодальная модель патогенеза детерминирует существование двух клинико-патофизиологических фенотипов данного состояния: анафилактического (дистрибутивный шок) и эмболического (обструктивный шок). Оба фенотипа связаны с развитием коагулопатии, крайним выражением которой является реализация тромботических катастроф. Пути реализации тромботических осложнений зависят от клинико-патофизиологического фенотипа данного критического состояния: при анафилактическом фенотипе они связаны с процессом микротромбогенеза, а при эмболическом как с микротромбогенезом, так и фибриногенезом. В первом клиническом случае представлено развитие синдрома имплантации костного цемента через механизм анафилаксии. У мальчика был установлен цементный спейсер после первичного удаления остеосаркомы бедренной кости. Мы предполагаем, что в этот период времени произошла сенсибилизация. Этот факт подтверждается наличием признаков реакции надкостницы в верхней трети правой бедренной кости по данным компьютерной томографии. Во время применения костного цемента при эндопротезировании коленного сустава возникли выраженные расстройства гемодинамики, сердечного ритма и оксигенации. Несмотря на характерный для данного патофизиологического фенотипа механизм микротромбогенеза, выраженной полиорганной недостаточности и реализации жизнеугрожающих тромботических осложнений удалось избежать благодаря эффективно проведенным противошоковым мероприятиям и раннему началу гепаринотерапии. Второй клинический случай иллюстрирует эмболический фенотип синдрома имплантации костного цемента. У мальчика с остеогенной саркомой большеберцовой кости при применении костного цемента во время эндопротезирования возник эпизод гипотензии, тахиаритмии, десатурации и гипокапнии. После операции сохраняется десатурация и по данным компьютерной томографии выявлены пристеночный дефект левой ветви легочной артерии и признаки обструкции сегментарных ветвей легочных артерий обоих легких, высокий уровень D-димера, эхопризнаки увеличения давления в правых отделах сердца. На 20-е сутки после операции отмечается нормализация сатурации при дыхании воздухом. По данным компьютерной томографии дефект заполнения левой легочной артерии отсутствует, но сохраняются признаки обструкции ветвей легочной артерии в верхней и средней доле справа, в нижней доле левого легкого. Таким образом, гемодинамическая катастрофа эмболического фенотипа синдрома имплантации костного цемента представляет собой классическую картину обструктивного шока с последующим развитием тромботических осложнений, благодаря объединению механизмов микротромбогенеза и фибриногенеза. Предложенное нами патогенетическое фенотипирование синдрома имплантации костного цемента позволяет разработать цель-ориентированную стратегию профилактики и лечения гемодинамических и тромботических проявлений этого состояния. Данный подход представляется актуальным и способным снизить частоту неблагоприятных исходов и осложнений.

Ключевые слова: синдром имплантации костного цемента; фенотипы патогенеза тромбоза; дети; интенсивная терапия; онкологические заболевания; клинические наблюдения.

Как цитировать

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儿童肿瘤患者骨水泥植入综合征的病理生理表型及临床观察

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摘要

儿童肿瘤患者的骨水泥植入综合征（bone cement implantation syndrome, BCIS）目前尚未得到充分研究。其多模式发病机制可分为两种临床病理生理表型：过敏反应型（分布性休克）和栓塞型（阻塞性休克）。两种表型均与凝血病相关，其最严重的表现形式为血栓危象。血栓形成的具体机制取决于该综合征的病理生理表型：过敏性表型主要涉及微血栓形成；栓塞性表型既涉及微血栓形成，也涉及纤维蛋白形成。病例 1（过敏性表型）：本病例展示了骨水泥植入综合征通过过敏机制发展的过程。一名男孩因股骨骨肉瘤接受原发性肿瘤切除术后植入骨水泥间隔器（cement spacer）。我们推测，在此阶段可能发生了致敏反应。这一推测得到了计算机断层扫描（CT）结果的支持，具体表现为右股骨上段骨膜反应的存在。在膝关节置换术中应用骨水泥后，患儿出现严重的血流动力学紊乱、心律失常和氧合障碍。尽管该表型的典型机制为微血栓形成，但得益于有效的抗休克治疗和早期肝素抗凝治疗，成功避免了严重的多器官功能衰竭和危及生命的血栓形成并发症。病例 2（栓塞性表型）：本病例展示了骨水泥植入综合征的栓塞性表型。另一名男孩因胫骨成骨肉瘤接受膝关节置换术，在术中骨水泥植入后，出现低血压、心动过速性心律失常、低氧血症和低碳酸血症。术后患儿持续出现低氧血症，CT检查显示左肺动脉分支壁缺损，并存在双肺段动脉分支阻塞；D-二聚体水平升高，超声心动图提示右心腔压力增高。术后第20天，患儿吸空气时血氧饱和度恢复正常。CT检查显示左肺动脉的填充缺损消失，但右肺上叶、中叶及左肺下叶的肺动脉分支仍存在阻塞。该病例表明，栓塞性BCIS的血流动力学危象表现为典型的阻塞性休克，并且微血栓形成与纤维蛋白生成的协同作用导致了血栓并发症的发生。本研究提出的BCIS病理生理表型分类有助于制定针对性预防和治疗策略，以优化血流动力学管理并降低血栓相关并发症的发生率。该方法具有重要临床价值，并可能降低不良结局及并发症的发生率。

关键词：骨水泥植入综合征；血栓形成机制表型；儿童；重症监护；肿瘤疾病；临床观察。

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BACKGROUND

Bone cement is used in the surgical treatment of bone cancer, to fill bone defects, to form temporary endoprostheses, and to fix metal structures. In most cases, bone cement is used in morbid bones, which require uniform load distribution, good quality of prosthesis fixation, and guaranteed reduction of the risk of periprosthetic fractures. Liquid methyl methacrylate monomer and powdered copolymer are the main components of bone cement. When mixed together, the liquid and powder undergo an exothermic reaction and solidify to form polymethyl methacrylate. Bone cement often contains various components such as antibiotics, radiopaque agents, cell growth factors, antiinflammatory, and anticancer agents [1]. Unfortunately, this fixation technique is associated with the risk of bone cement implantation syndrome (BCIS), which is characterized by hypoxemia, hypotension, cardiac arrhythmias, and increased pulmonary vascular resistance [2]. Circulatory arrest requiring cardiopulmonary resuscitation is the most severe symptom of this condition. This condition may occur at any stage of endoprosthesis surgery, from prosthesis implantation to rehabilitation [3].

BCIS is diagnosed in 26%–74% of cancer patients over 18 years of age [4, 5]. It remains poorly understood in pediatric practice, especially in children with cancer. In 2009, a severity classification for this complication was proposed, which includes hypoxemic syndrome and systemic hemodynamic disorder [6]. The classification is relevant, but largely retrospective due to the actual diagnosis of clinical symptoms. However, the BCIS pathogenesis is unclear and is not considered in this classification.

This *article aims* to present the concept of pathogenetic phenotyping of BCIS using pediatric cancer cases.

THE CONCEPT OF PATHOGENETIC PHENOTYPING OF BONE CEMENT IMPLANTATION SYNDROME

It is suggested that a combination of direct toxicity of materials and/or activation of IgE-mediated and non-IgE-mediated anaphylactic mechanisms may lead to BCIS. In addition to mechanical obstruction, material embolization associated with high intramedullary pressure during prosthesis placement with subsequent endothelial damage is considered another possible pathogenesis of BCIS [3]. Emboli of bone cement, fat, and bone promote the release of endothelin-1, anaphylatoxins C3a and C5a, serotonin, tissue thromboplastin, thrombin, thromboxane A2, platelet-activating factor, adenosine diphosphate, platelet-derived growth factor, and other vasoactive substances from the endothelium of pulmonary vessels, resulting in pulmonary vasoconstriction, a decrease in systemic vascular resistance, and, of course, a decrease in cardiac output [7]. In addition, direct endothelial damage, complement activation, systemic inflammatory response, platelet activation, dysregulation of coagulation factor generation, and altered fibrinolysis induce coagulopathy. Clinical manifestations may include micro- and macrothrombotic complications.

Therefore, in addition to the potentially reversible generalized hemodynamic catastrophe during surgery, there is a high risk of local perfusion disorders during bone cement use, which may lead to severe postoperative multiple organ failure and fatal complications. This is supported by scientific publications, with intraoperative mortality rate for BCIS ranging from 0.16% to 0.68%, 30-day mortality rate from 2.5% to 9.0%, and one-year mortality rate from 21.0% to 94.1% [8].

We suggest that the multimodal pathogenetic model of BCIS implies two clinical and pathophysiological BCIS phenotypes, including anaphylactic (distributive shock) and embolic (obstructive shock). Both phenotypes are associated with hypercoagulability syndrome, with thrombotic catastrophes representing their most severe manifestation. In the anaphylactic phenotype, the endothelial layer is damaged, and microthrombogenesis occurs via activation of unusually large von Willebrand factor and platelets. In the embolic phenotype, damage to both the endothelial and subendothelial layers activate microthrombogenesis (von Willebrand-dependent coagulation pathway) and fibrinogenesis (tissue factor-dependent coagulation pathway). Both conditions may lead to macrothrombosis, resulting in local and/or generalized postoperative hemodynamic catastrophe [9]. This concept is consistent with the publications on the pathophysiology of BCIS and its generally accepted clinical classification [1–10]. Fig. 1 shows our pathogenetic phenotyping of BCIS.

CASE DESCRIPTION

Case description 1

A 12-year-old boy (weight 45 kg, height 147 cm) was diagnosed with malignant neoplasm of lower limb long bones, conventional osteosarcoma of distal epimetadiaphysis of right femur, osteoblastic disease with bilateral metastatic lung lesions $T_2N_0M_{1a}$, AJCC (American Joint Committee on Cancer) stage IVA, and admitted for surgery in June 2023. Medical history showed that the disease onset was in April 2022, when the child first complained of pain in the right knee joint. Magnetic resonance imaging revealed a femur lesion and effusion in the knee joint cavity. Puncture biopsy showed conventional osteoblastic osteosarcoma. Positron emission computed tomography with 18-fluorodeoxyglucose demonstrated metabolically active tumor tissue in a mass lesion of the distal epimetadiaphysis of the right femur, with secondary changes in the right external iliac and inguinal

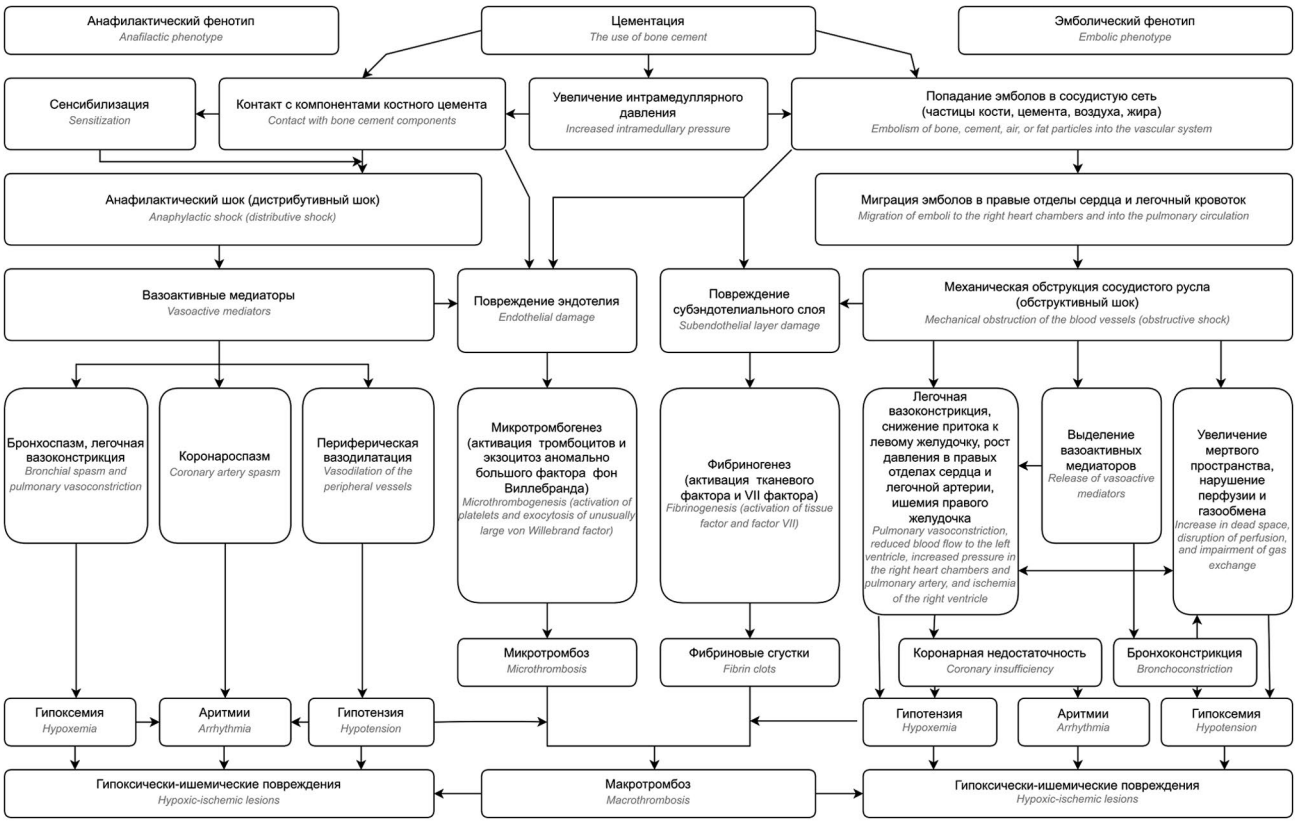


Fig. 1. Pathogenetic phenotyping of bone cement implantation syndrome.
Рис. 1. Патогенетическое фенотипирование синдрома имплантации костного цемента.

lymph nodes. Mass lesions in lung parenchyma without contrast agent accumulation were also identified. Five cycles of neoadjuvant polychemotherapy were administered according to the EURAMOS protocol.

In September 2022 in "Dmitry Rogachev National Medical Research Center of Pediatric Hematology, Oncology, and Immunology", the patient underwent surgery to remove the tumor of the distal right femur and replace the defect with a cement spacer. Histological examination of the excised tumor revealed osteosarcoma with grade II therapeutic pathomorphism (necrosis and organization slightly over 60%). Chest multislice computed tomography (MSCT) revealed multiple secondary parenchymal lesions in both lungs. Right thoracotomy, exploratory surgery of the right lung, atypical resection of the right lung, and partial removal of metastatic lesions were performed. Postoperative MSCT showed thrombi in the lumen of the right lower lobe pulmonary artery and its branches in addition to the remaining small metastatic lesions. A total of six HD I cycles of polychemotherapy were administered.

In December 2022, signs of periosteal reaction were found in the upper third of the right femur. In February 2023, left thoracotomy was performed with exploratory surgery of the left lung and removal of the lesions from the left lung. In May 2023, a bronchial blocker was placed in the left lower lobe bronchus, and left pleural drainage was performed.

A preoperative evaluation in June 2023 revealed no abnormalities in standard laboratory tests. Hemostasis parameters were within reference ranges. The patient did not have any other medical conditions except for grade I respiratory failure. Lung MSCT showed metastatic lesions, total atelectasis of the left lower lobe, left hydropneumothorax, and postoperative changes in the left upper lobe. The pleural cavity was drained, and the pleural drainage was removed 6 days prior to surgery.

Surgical removal of the cement spacer followed by knee arthroplasty with the placement of a Mutars Implantcast modular prosthesis was performed over 9 hours under combined endotracheal anesthesia (including insufflation of sevoflurane at 1 minimum alveolar concentration, infusion of fentanyl at 2 μg/kg/h and rocuronium bromide at 0.3 mg/kg/h). Antibacterial prophylaxis included cefuroxime at 50 mg/kg every 4 hours and vancomycin at 15 mg/kg every 6 hours. Tranexamic acid at 15 mg/kg and omeprazole at 40 mg were administered before surgery. At the early stages of anesthesia, the fluid deficit was replenished with 1500 mL, followed by 300 mL/h infusion. The femoral artery was injured during isolation and removal of the cement spacer. Autovein was used to restore its integrity. Blood loss was 900 mL, representing 28.5% of the patient's circulatory blood volume. Laboratory monitoring showed a decrease in hemoglobin to 86 g/L. During norepinephrine infusion at 0.05 μg/kg/min,

hemodynamics were stable. Blood loss was replaced with 1000 mL of sterofundin and transfusion of 610 mL of red blood cell suspension. Ultrasound showed arterial blood flowing. Heparin was administered at 30 U/kg, followed by infusion at 10 U/kg/h. Activated partial thromboplastin time (APTT) of 190 seconds was achieved. A knee arthroplasty was performed later during surgery. During bone cement administration, the patient had hypotension of up to 30/28 mmHg, bradyarrhythmia with a heart rate of 20 bpm, and desaturation up to 80%. Closed chest compressions were performed. Adrenaline at 0.1 mg and dexamethasone at 12 mg were administered intravenously. Volume support was provided with 1000 mL sterofundin and 100 mL albumin. Vasopressor therapy with norepinephrine was increased to 0.3 μg/kg/min. Mechanical ventilation with 100% oxygen was performed. Therapy restored hemodynamics and oxygenation within 3 minutes. APTT was re-measured and was 41 seconds, so heparin infusion was increased to 15 U/kg/h. Arthroplasty was completed. Total blood loss was 32% of the circulating blood volume (1000 mL). The volume of intra-operative infusion and transfusion was 6500 mL. Intra-operative urine output ranged from 4 to 6 mL/kg/h, total urine output was 3450 mL.

After surgery, the patient was transferred to the intensive care unit on mechanical ventilation with norepinephrine infusion at 0.2 μg/kg/min, where he stayed in drug-induced sleep for 24 hours. No increased bleeding from the surgical wound or blood flow through the drainage was observed. On Day 2, echocardiography showed no decrease in myocardial contractility, creatine kinase MB was 11.9 U/L, and lung radiography showed no changes from the preoperative pattern. Vasopressor support was discontinued, and the patient was removed from mechanical ventilation and extubated. Ultrasound showed good femoral blood flow in the operated limb. Limb saturation was 100% on air. APTT was 59 seconds with heparin infusion at 12.5 U/kg/h.

On postoperative day 4, the patient was transferred to a specialized unit. The level of respiratory failure was similar to preoperative. No other signs of organ failure were observed. On day 6, anticoagulant therapy with heparin was discontinued. No antiplatelet therapy was used. On day 9, lung MSCT was comparable to preoperative MSCT. No new lesions (thrombi, emboli) were detected in the lung tissue and vessels. On postoperative day 10, the patient was discharged for further follow-up at the local healthcare facility.

In November 2023, the patient underwent left rethoracotomy, subtotal pneumolysis, resection of the basal pyramid of the lower left lung lobe, and atypical resection of the S6 left lung at the Dmitry Rogachev National Medical Research Center of Pediatric Hematology, Oncology, and Immunology. The postoperative period was unremarkable. Histological examination of the resected lung tissue showed no bone cement particles. The patient is currently alive and has no adverse effects caused by intra-operative BCIS.

Case description 2

An 11-year-old boy (body weight 51.5 kg, height 142 cm) was diagnosed with conventional fibroblastic osteosarcoma of the upper third of the left tibia, stage $T_2N_0M_{1a}$ IV A according to AJCC and admitted for surgery in June 2023. Medical history revealed that the patient received treatment for a tibia fracture following a sports injury in March 2022. In August 2022, he received medical care for a recurrent tibial fracture. In September 2022, an extended in-hospital evaluation with limb MSCT found an osteolytic lesion with soft tissue and intraosseous components in the upper third of the left tibia. Positron emission tomography revealed a hypermetabolic mass lesion with evidence of osteodestruction in the upper third of the left tibia. The lesion was biopsied. Histological examination revealed high-grade fibrosarcoma. Chest CT confirmed metastases in S3, S6, S9, S10 of the right lung and S2, S8 of the left lung. Since October 2022, 6 cycles of polychemotherapy have been performed according to the EURAMOS protocol. In January 2023, the tumor was removed from the proximal left tibia, and the defect was repaired with a cement spacer. The histological diagnosis was confirmed. The patient experienced an allergic rash after receiving cefuroxime and vancomycin. Since February 2023, 5 additional cycles of polychemotherapy have been performed according to the EURAMOS protocol. Bilateral thoracotomy and metastasectomy were performed in May 2023. In June 2023, the patient was stable, and standard preoperative laboratory tests showed no evidence of multiple organ failure, coagulopathy, or abnormal major vessel flow. Preoperative hemoglobin was 92 g/dL.

During 4-hour surgery, the cement spacer in the left tibia was removed, and knee arthroplasty with a Stanmore JTS extendable prosthesis was performed. Prolonged epidural anesthesia (morphine at 0.05 μg/kg during catheter placement, then prolonged infusion of 0.2% ropivacaine at 0.2 mg/kg/h) and combined endotracheal anesthesia (insufflation with a minimum alveolar concentration of sevoflurane, infusion of fentanyl at 0.5 μg/kg/h and rocuronium bromide at 0.3 mg/kg/h) were administered. Antibacterial prophylaxis included clindamycin at 10 mg/kg and amikacin at 15 mg/kg. Tranexamic acid at 15 mg/kg and omeprazole at 40 mg were administered before surgery. At the initial phase of anesthesia, hypovolemia was treated with infusion of norepinephrine at 0.05 μg/kg/min. The fluid deficit was replenished with 1200 mL, followed by infusion at 300 mL/h. During knee replacement and cement placement, the patient experienced hypotension of up to 70/40 mmHg, tachyarrhythmia with a heart rate of 132–135 per minute, hypocapnia of up to 30 mmHg, and desaturation up to 85%. Mechanical ventilation was performed with 100% oxygen. Volume support included 1000 mL sterofundin. Vasopressor therapy with norepinephrine was increased to 0.15 μg/kg/min. Therapy restored hemodynamics and oxygenation within 5 minutes.

Arthroplasty was continued. Intra-operative blood loss was 170 mL (5% of the patient's circulatory blood volume). A transfusion of 320 mL red blood cell suspension was performed. After transfusion, hemoglobin was 115 g/L. The volume of intra-operative infusion and transfusion was 3400 mL. Intra-operative urine output ranged from 5 to 6 mL/kg/h, total urine output was 1300 mL. When surgery was completed, vasopressor support was discontinued, and the patient was removed from mechanical ventilation and extubated. Hemodynamics were stable, and spontaneous respiration was adequate. With oxygen support of 6 L/min, saturation was 100%. On air, desaturation was up to 88%–94%. The patient was transferred for MSCT, which showed a parietal defect in the left pulmonary artery, contrast defects in the segmental branches of the right and left pulmonary arteries (Fig. 2), and peribronchial infiltration of the right lung with evidences of lymphostasis (interstitial edema).

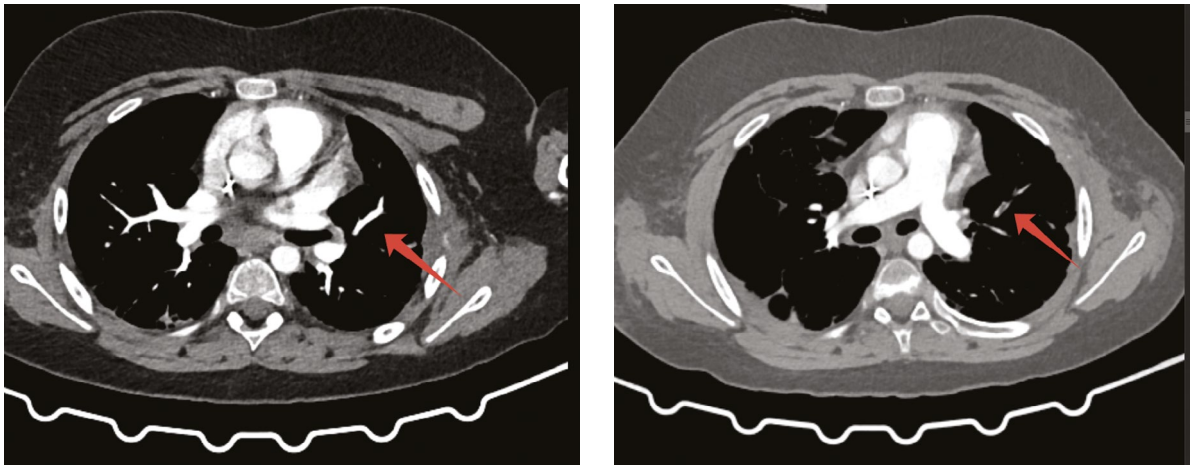
The patient was transferred to the surgical unit, where oxygen support was continued for 3 days. An examination revealed D-dimer level of 2610 ng/ml, antithrombin III level of 78%, APTT of 26.5 seconds. Ultrasound of the inferior vena cava and deep and superficial veins of the lower limbs showed no patency or blood flow abnormalities. Thrombolysis was not performed due to the patient's stable condition. Anticoagulant therapy was prescribed with enoxaparin sodium 5000 IU subcutaneously every 12 hours. On postoperative day 2, echocardiography showed normal-sized heart chambers, the left ventricular ejection fraction by the Teichholz method of 63.1%, and a tricuspid annular plane systolic excursion of 24 mm (above the reference value of 18.3 mm for the age of 11 years). The major vessels were patent, the valves were unchanged, and the septa were intact. Desaturation up to 88%–94% on air maintained for four days. On postoperative day 3, D-dimer level was 660 ng/mL, anti-Xa factor activity was 0.49 IU/mL. On day 5, saturation was 97% on air. The patient was transferred to the oncohematology unit for 6 cycles of polychemotherapy according to the EURAMOS protocol. On postoperative day 20, there was no evidence of respiratory failure, and the patient was considered stable. Lung MSCT showed resolution of the previously identified defect in contrast enhancement of the left pulmonary artery.

In January 2024, negative changes were observed, including multiple metastatic lesions in the lung parenchyma. The patient received anti-relapse therapy and specific polychemotherapy. In June 2024, left thoracotomy was performed with removal of left lung lesions. Histological examination showed a metastatic lung lesion with the osteosarcoma substrate, without evidence of therapeutic pathomorphism. At some sites, resection margins were tumor-positive. Bone scintigraphy with Tc99 suggested a lesion of contrast agent accumulation in the posterior left third rib with periosteal reaction. The prognosis was considered unfavorable considering failure of surgical remission. The patient qualified for palliative care.

DISCUSSION

The presented clinical cases demonstrate two possible pathogenetic phenotypes of BCIS.

In the first case, prior to development of BCIS, blood loss was completely compensated, hemodynamics were stable, and no arrhythmia or desaturation was observed. After the use of bone cement, hemodynamic, arrhythmic, and oxygenation disorders occurred, which are typical for this grade 3 anaphylactic BCIS according to the Donaldson classification [6]. We suggest that sensibilization occurred during the initial use of bone cement, which is indirectly confirmed by the signs of periosteal reaction in the upper third of the right femur on the pre-arthroplasty CT scan. Repeated



a *b*

Fig. 2. Comparison of computed tomographic pulmonary angiography images before (*a*) and after surgery (*b*). Arrow indicates the segmental branch of the left pulmonary artery without a filling defect and with a filling defect following pulmonary embolism.
Рис. 2. Сравнение изображений компьютерной ангиографической томографии легких до (*a*) и после операции (*b*). Стрелкой показана сегментарная ветвь левой легочной артерии без дефекта заполнения и с дефектом заполнения после эмболии легочной артерии.

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contact with cement components led to the release of vasoactive mediators such as histamine, serotonin, bradykinin, eicosanoids, anaphylatoxins C3a and C5a, endothelin-1, etc. into the bloodstream. These mediators caused a decrease in peripheral vascular resistance, pulmonary and coronary vasoconstriction, bronchospasm, decreased venous return and, consequently, cardiac output [11, 12]. Clinical manifestations of this condition included severe hypotension, bradyarrhythmia, and desaturation. Unfortunately, blood tryptase was not monitored.

The sharp decrease in APTT from 190 to 41 seconds during heparin infusion should also be mentioned. This suggests a potentially thrombogenic situation. Despite cancer with lung lesions, history of potentially thrombogenic thrombotic damage to the pulmonary blood flow and hemodynamic catastrophe, MSCT showed no new lesions (thrombi, emboli) in the lung tissue and vessels. This may be explained by effective and rapid treatment of distributive shock and early initiation of heparin therapy. This combination of factors in the anaphylactic phenotype of BCIS may reduce the risk of significant thrombotic events. However, there is another opinion. A retrospective study performed by García-Mansilla et al. [13] in a cohort of adult patients after total hip arthroplasty found that intraoperative administration of unfractionated heparin increased the risk of BCIS by 17-fold and did not reduce the risk of thromboembolic complications within 30 days post surgery. Heparin may increase the risk of fat embolism, but in this case there was no evidence of postoperative thromboembolic complications [14]. Cases of anaphylaxis were reported with heparin, but the patient had previously received heparin therapy several times, and no such reactions were reported [15].

The second clinical case represents embolic BCIS of grade II according to the Donaldson classification [6]. The patient did not experience respiratory failure, thrombotic complications, or coagulopathy, although he had cancer with metastatic lung disease and underwent preoperative polychemotherapy. During the surgery, emboli (particles of cement, bone tissue, fat, or air) were thought to enter the blood stream through damaged bone tissue structures due to increased intramedullary pressure during cement placement. The emboli reached the heart and pulmonary circulation. Pulmonary vasoconstriction, increased pulmonary artery and right ventricular pressures, decreased left ventricular inflow, left ventricular compression by the right ventricle, decreased cardiac output, and decreased coronary blood flow resulted in hypoxia, hypotension, and arrhythmias [3, 6]. Deterioration of regional circulation, damage to the endothelium and subendothelial layers by the embolus, activation of the hemostasis system and platelets resulted in thrombotic occlusion at the site of embolus dislocation [10]. This fact was confirmed by CT performed immediately after the bone cementing surgery. It showed a defect in contrast enhancement of the left pulmonary artery with contralateral edema of the right lung, as well as smaller defects in contrast enhancement of the segmental branches of the right and left pulmonary arteries. In addition, the patient had postoperative air desaturation, high D-dimer levels, and echo evidence of increased pressure in the right chambers of the heart.

Therefore, the hemodynamic catastrophe in the embolic BCIS represents classic obstructive shock with subsequent thrombotic complications.

CONCLUSION

BCIS can manifest as two clinical and pathophysiologic phenotypes—anaphylactic (distributive shock) and embolic (obstructive shock). The risk of thrombotic catastrophe in BCIS depends on the pathogenesis of this critical condition. In the anaphylactic phenotype, the risk is driven by microthrombogenesis, and both microthrombogenesis and fibrinogenesis are involved in the embolic phenotype. The proposed pathogenetic phenotyping of BCIS allows for a targeted approach to prevent and treat hemodynamic and thrombotic complications in affected patients. This approach appears to be relevant and has the potential to reduce the incidence of adverse outcomes and complications.

ADDITIONAL INFO

Authors' contribution. N.P. Leonov, anesthesiology support during surgical interventions, developed the concept of the article, data analysis, literature review, writing the text; V.A. Leonova, collection of clinical material, developed the concept of the article, literature review, writing the text; V.V. Shchukin, coordination of anesthesiology service, developed the concept of the article, collected information, edited the text; A.P. Scherbakov, analysis of MSCT study data, preparation of the image for publication; P.G. Madonov, V.V. Lazarev, E.A. Spiridonova, analysis and generalization of the obtained results of the publication, editing of the publication text, development of the concept; N.S. Grachev, organization of clinical and scientific work, development of the concept, financing of the publication, editing of the publication text, scientific guidance. The authors have approved the version for publication and have also agreed to be responsible for all aspects of the work, ensuring that issues relating to the accuracy and integrity of any part of it are properly considered and addressed.

Ethical review. Not applicable.

Consent for publication. The authors received written informed voluntary consent from patients to publish personal data in a scientific journal, including its electronic version. The scope of published data was agreed with the patients.

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Generative AI. Generative AI technologies were not used for thisarticle creation.

ДОПОЛНИТЕЛЬНАЯ ИНФОРМАЦИЯ

Вклад авторов. Н.П. Леонов — анестезиологическое обеспечение во время хирургических вмешательств, разработчик концепции, анализ данных, обзор литературы, написание текста; В.А. Леонова — сбор клинического материала, разработчик концепции, обзор литературы, написание текста; В.В. Щукин — координирование работы анестезиологической службы, разработка концепции, сбор информации, редактирование текста; А.П. Щербаков — анализ данных МСКТ-исследования, подготовка изображения к публикации; П.Г. Мадонов, В.В. Лазарев, Е.А. Спиридонова — анализ и обобщение полученных результатов публикации, редактирование текста публикации, разработка концепции; Н.С. Грачев — организация клинической и научной работы, разработке концепции, финансирование издания, редактирование текста публикации, научное руководство. Авторы одобрили версию для публикации, а также согласились нести ответственность за все аспекты работы, гарантируя надлежащее рассмотрение и решение вопросов, связанных с точностью и добросовестностью любой ее части.

Согласие на публикацию. Авторы получили письменное информированное добровольное согласие законных представителей пациентов на публикацию персональных данных в научном журнале, включая его электронную версию Объем публикуемых данных с законными представителями пациентов согласован.

Источники финансирования. Отсутствуют.

Раскрытие интересов. Авторы заявляют об отсутствии отношений, деятельности и интересов за последние три года, связанных с третьими лицами (коммерческими и некоммерческими), интересы которых могут быть затронуты содержанием статьи.

Генеративный искусственный интеллект. При создании настоящей статьи технологии генеративного искусственного интеллекта не использовали.

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