The First Experience of Conducting the Anesthetic Support During a Simultaneous Surgery in a Kindler Syndrome Patient

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ABSTRACT

BACKGROUND: *Kindler syndrome is a rare autosomal recessive disease, one of the forms of congenital epidermolysis bullosa. Clinically, the disease manifests by the development of bubbles on the skin and mucosal membranes with further cicatrization, as well as by the development of narrowing in the esophagus, the urethra, the vagina and the urinary ducts. In the presented clinical case of the first ever in Russia conducted simultaneous surgery in the settings of general combined anesthesia in a patient with Kindler syndrome, evaluation was carried out for the criteria of difficult airways, special attention was paid to the method of conducting the endotracheal intubation, to monitoring the vital functions of the organism and to following the multimodal analgesia principle. Due to the high risk of post-operative nausea and vomiting, a necessity was justified for increasing the antiemetic effect.* ***CLINICAL CASE DESCRIPTION:*** *The main indications to conducting the surgery in a female patient aged 49 years with congenital epidermolysis bullosa (Kindler syndrome) were the complaints of significant difficulties and pain upon swallowing, decreased appetite, presence of dysphagia with a background of inhomogeneous circular narrowing of the esophagus, pain when moving the eyes and the absence of nasal breathing with a background of nasal vestibule atresia. The main tasks of surgical treatment were the elimination of incapacitating complications and improving the quality of life for the patient. The multiplicity of stages in the treatment process was deemed impractical due to the necessity of conducting three anesthetic support procedures with high risk of additional damaging the oropharynx and upper airways during tracheal intubation, due to which, a decision was drawn up on arranging a simultaneous surgical treatment of complications of the main disease. The duration of surgery was 195 minutes, while the anesthesia lasted for 210 minutes. The performed procedures included the elimination of eyelid eversion, the dissection of symblepharon, the excision of the nasal vestibule atresia and the endoscopic dilation of esophageal stricture. The postoperative period was uncompromised with reported restoring the functioning of nasal breathing, of the visual organs and with the elimination of dysphagia. Upon the examination conducted 11 months after surgery, there were no signs of recurrence of the eliminated complications of the main disease.* ***CONCLUSION:*** *Increasing the safety and preventing the iatrogenic complications during the course of anesthesia in patients with epidermolysis bullosa is the most important task. The development of modern medical technologies with using the microsurgical and the endoscopic methods along with the personalized approach in selecting the anesthetic support allow for wider usage of simultaneous surgeries in the treatment of complications in Kindler syndrome patients.*

Keywords: *Kindler syndrome; epidermolysis bullosa; difficult airways; general anesthesia; stricture dilation; endoscopic balloon dilation.*

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BACKGROUND

Kindler syndrome is one of the four types of congenital epidermolysis bullosa, being a very rare autosomal recessive genodermatosis. As of today, in the whole world, there are approximately 400 registered cases of the disease [1]. Among the main clinical manifestations of this disease are the formation of bubbles on the skin and the mucosal membranes from the moment of birth after a minimal injury, generalized progressive poikiloderma, photosensitivity, pseudosyndactyly, narrowing of the esophagus, of the urethra, of the vagina and of the urinary ducts, as well as colitis and esophagitis [2]. The often reported signs include the dystrophy of nail plates, the ectropion in the lower eyelids, keratoderma, fibrotic finger constrictions, impaired sweating (anhidrosis or hypohidrosis), leukokeratosis of the lips, ulcers in the buccal mucosa and in the hard/soft palate [3].

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Первый опыт проведения анестезиологического пособия при симультанной операции у пациентки с синдромом Киндлера

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АННОТАЦИЯ

Обоснование. *Синдром Киндлера — редкое аутосомно-рецессивное заболевание, одна из форм врождённого буллёзного эпидермолиза. Клинически заболевание проявляется образованием пузырей на коже и слизистых оболочках с последующим рубцеванием, а также развитием сужений пищевода, уретры, влагалища и мочеточников. В представленном случае первой в России симультанной операции в условиях общей комбинированной анестезии у пациентки с синдромом Киндлера оценены критерии трудных дыхательных путей, особое внимание уделено методике выполнения эндотрахеальной интубации трахеи, мониторингу витальных функций организма, соблюдению принципа мультимодальной анальгезии. В связи с высоким риском послеоперационной тошноты и рвоты обоснована необходимость усиления антиэметического эффекта.*

Описание клинического случая. *Основными показаниями к выполнению операции у пациентки в возрасте 49 лет с врождённым буллёзным эпидермолизом (синдром Киндлера) явились жалобы на выраженное затруднение и боль при глотании, снижение аппетита, наличие дисфагии на фоне неравномерного циркулярного сужения пищевода, болезненность при движении глаз, отсутствие носового дыхания на фоне атрезии преддверия носа. Основными задачами оперативного лечения были устранение инвалидизирующих осложнений и улучшение качества жизни пациентки. Многоэтапность в лечении была признана нецелесообразной ввиду необходимости выполнения трёх анестезиологических пособий с высоким риском дополнительных повреждений ротоглотки и верхних дыхательных путей при интубации трахеи, в связи с чем принято решение о симультанном оперативном лечении осложнений основного заболевания. Длительность операции составила 195 минут, анестезии — 210 минут. Выполнено устранение выворота век, рассечение симблефарона, иссечение атрезии преддверия носа и эндоскопическая дилатация стриктуры пищевода. Послеоперационный период протекал благоприятно, отмечено восстановление функции носового дыхания, органов зрения и устранение дисфагии. При обследовании через 11 месяцев после операции признаков рецидива устранённых осложнений основного заболевания не выявлено.* ***Заключение.*** *Повышение безопасности и профилактика ятрогенных осложнений во время проведения анестезии у пациентов с буллёзным эпидермолизом является важнейшей задачей. Развитие современных медицинских технологий с использованием микрохирургических и эндоскопических методик, персонализированного подхода в выборе анестезиологического пособия позволяют более широко использовать симультанные операции в лечении осложнений у пациентов с синдромом Киндлера.*

Ключевые слова: *синдром Киндлера; буллёзный эпидермолиз; трудные дыхательные пути; общая анестезия; дилатация стриктур; эндоскопическая баллонная дилатация.*

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The presence of epidermolysis bullosa in patients classifies them as the individuals with predictable difficult airways, which pre-determines a large number of specific features both when preparing and conducting the surgery, as well as during the post-operative management. Among the main problems of the surgical period that are worth noting, there are difficulties when ventilating by means of a face mask, by direct laryngoscopy and by intubation.

Until the present moment in Russia and worldwide, there were no presented cases of anesthetic management of simultaneous surgeries in adult patients with Kindler syndrome. Our article has demonstrated the first experience of simultaneous surgery in

a patient with congenital epidermolysis bullosa (Kindler syndrome) with an accent to specific features of conducting the combined general anesthesia.

CLINICAL CASE DESCRIPTION

Patient information

Female patient B., aged 49 years, hospitalized to the Burn Department with Plastic Surgery Unit of the Federal State Budgetary Institution "The Nikiforov's Russian Center of Emergency and Radiation Medicine" under the Ministry of the Russian Federation for Civil Defence, Emergencies and Disaster Relief.

The anthropometrical data were the following: body length 156 cm, body weight 47 kg, body mass index 19.31 kg/m^2.

Case history. The patient has the disease from the moment of birth. She was born in a multi-child family, being the outcome of her mother's 10th pregnancy. Twelve months after birth, her skin started having bubbles, both spontaneously and after insignificant injuries. From the age of 5 years she started noting the adhesions in her fingers. From the age of 10 years, besides dizziness, palpitations and increased sweating at the open sun, she started noting gradual worsening of microstomia. According to the data from histological and genetical testing, the Kindler syndrome was confirmed. Pathological mobility of teeth, reported from the age of 16 years, has led to their further painless loss until complete edentia (incapable of wearing the prostheses due to traumatizing the oral cavity mucosa). At the age of 27, there was an episode of grade IV dysphagia with a background of a foreign body in the esophagus: she underwent mediastinotomy with removing the foreign body from the esophagus and with further draining. Due to having a syndactyly in her palms, she was operated at the age of 6, then at 17 and 20 years with grafting the cleaved transplants. At the age of 35 years, upon examination, hydronephrosis was found in the right kidney, in 2021 she underwent stenting of the right urinary duct. From the age of 40, the patient was noting the difficulty of nasal breathing and discomfort in the frontal area caused by narrowing of the nasal passages. In 2020 she underwent the dissection of synechias and the excision of strictures in her left nasal passage. At the present moment, the patient is using silicone dilators for preventing the recurrence. Comparing to the hospitalization in 2021, significant worsening is reported for the condition of the eyes due to the progression of conjunctival adhesions.

The main indication for conducting the surgery was the complaints from the patient of significant difficulties and pain upon swallowing, aggravating in the morning (due to which, only the intake of liquid foods was possible); decreased appetite; presence of grade III–IV dysphagia (Bown scale) with a background of inhomogeneous circular narrowing of the esophagus at the level of the bodies of C7–Th1 vertebral bones with a length of up to 8.6 mm and with the maximal narrowing of the lumen up to 1.6 mm according to the data from esophageal radioscopy; complaints of pain when moving the eyes, lacrymation and eye redness with a background of ectropion, subtotal symblepharon in the lower eyelid fornix, pseudopterygium in both eyes; absence of nasal breathing on the right side with a background of complete atresia of the nasal vestibule on the right side and partial atresia of the nasal vestibule on the left side.

Laboratory and instrumental diagnosis

The physical status of the patient corresponded to class II–III of the scale by the American Society of Anesthesiologists (ASA). The surgical intervention, by its extent and type, was considered as the surgery with moderate traumatic degree. Preoperative evaluation of the status of the upper airways has revealed the risk factors of difficult mask ventilation according to the MMMMASK scale (Mask seal due to the absence of teeth; Mallampati — class IV), difficult installation of the supraglottic air tube according to the RODS scale (R — limited opening of the mouth) and difficult direct laryngoscopy. The criteria for difficult airways were also determined: mouth opening — 2.9 cm (microstomia) (Fig. 1), large tongue, complete edentia, thyromental distance — 6 cm, sternomental distance — 9 cm, hyomental distance — 4.5 cm, Mallampati test — IV (Fig. 2), presence of chronic erosions in the oral cavity (Fig. 3).

Provisional diagnosis

Congenital epidermolysis bullosa, Kindler syndrome. Complete edentia. Microstomia. Chronic erosion of the hard palate. Dysphagia grade III–IV. Esophageal stenosis. Protein-energetic deficiency of moderate degree of severity. Chronic mild degree iron-deficient anemia. Autoimmune thyroiditis, nodular nontoxic goiter, subclinical hypothyroidism. Hypertensive disease stage II. Arterial hypertension grade I. Mild eccentric hypertrophy of the left ventricle. Hydronephrosis of the right kidney, chronic pyelonephritis.

Treatment

The main tasks of surgical treatment were the elimination of incapacitating complications and the improvement of the quality of life for the female patient.

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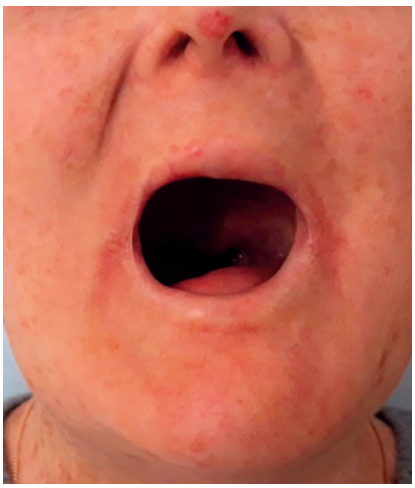

Fig. 1. Cicatricial stricture of the mouth with the formation of microstomia.

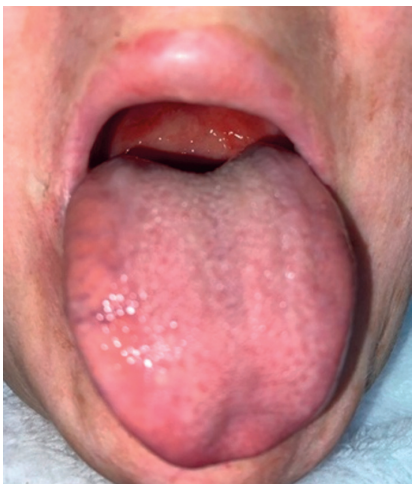

Fig. 2. Class IV oropharynx structure according to S.R. Mallampati.

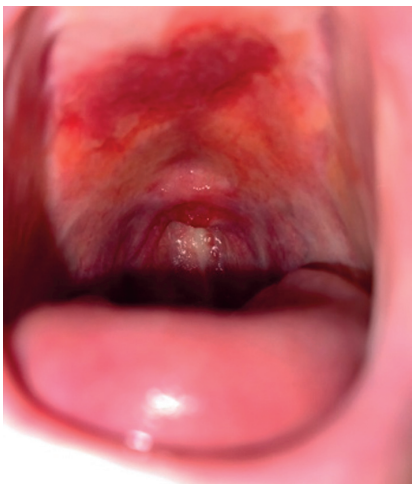

Fig. 3. Chronic erosion of the hard palate.

When planning the surgery, the multiplicity of stages in the treatment was deemed impractical due to the necessity of conducting three anesthetic support procedures with high risk of additional damaging the oropharynx and upper airways upon tracheal intubation. The traditional scales of evaluating the risk of difficult intubation — El-Ganzouri Risk Index, LEMON, Arne, MOSCOW-TD — were also inapplicable due to the absence of the possibility of measuring the distance between the incisors (complete edentia) as one of the important signs of predicting the difficult intubation. Thus, the patient was proposed to undergo simultaneous surgical treatment of complications of the main disease.

At the first stage, a microsurgical technique was used for dissecting the symblepharon with the elimination of pseudopterygium; other procedures included the application of amniotic covering; the external canthotomy in the left and the right eyes; the elimination of the eversion in the lower eyelid with the grafting of the free dermal flap to the left and the right eyes; the second stage included the dissection of the synechias in the nasal cavity on the left side and on the right side, the dilatation of the nasal valve on the left side with an installation of the rhinological splint containing the airway; at third stage, the procedures included the endoscopic balloon dilation of the cicatrical stricture in the upper third of the esophagus under the intra-operative radiology control.

Due to the specific features of the main disease, implementing the standard algorithm for achieving the passability of the upper airways was hampered. The anesthesiology support was conducted based on the general combined anesthesia with tracheal intubation and artificial pulmonary ventilation. As the temporary vascular access, 18G peripheral venous catheter was used, fixated to the skin with the Mepitac (Sweden) soft silicone-based non-adhesive patch. The premedication used included the administration of Dexamethasone at a dosage of 4 mg (calculated as 0.1 mg/kg), Metoclopramide 10 mg (calculated as 0.25 mg/kg). The preoxygenation with 100% oxygen fraction in the inhaled gas mixture (FiO_2) was performed for 3 minutes. The induction of anesthesia was initiated by means of consecutive intravenous injections of Propofol at a dosage of 100 mg (2–2.5 mg/kg), Fentanyl 0.2 mg (3–3.5 μg/kg) and Rocuronium bromide 20 mg (0.6 mg/kg). The anesthesia was maintained by the inhalation of Sevoflurane (minimal alveolar concentration 0.8–1.0%) and by the bolus injection of Fentanyl (1 μg) as needed during the traumatizing stages of surgical treatment. The oxygen fraction in the breathing mixture was 50% with the flow rate of anesthetic gas mixture being 1 l/minute. In order to minimize the injury inflicted to the mucosal membranes when conducting the intubation, water-based lidocaine gel was used — Cathejell (Austria).

For the purpose of preventing the damage of trachea by the cuff of the endotracheal tube, an optimal pressure was maintained in it. In order to conduct the intubation, the endotracheal tube made of Ivory-type soft polyvinyl chloride was used along with the No. 6.5 cuff. The cuff pressure was maintained using the manometry at the level minimally acceptable for hermetization — 20 cmH2O with controls every 15 minutes during the whole course of surgery. If necessary, cuff pressure correction was made.

The intubation of the trachea was done using the videolaryngoscopy method with the C-MAC

laryngoscope (Karl Storz, Germany) and the "D-BLADE" blade. The laryngoscopic findings corresponded to class IIa according to the Fremantle scale of the Cormack–Lehane classification system. The intubation employed the modified bougie method. The fixation of the endotracheal tube was performed using the wraps, protecting the skin with Mepilex (Sweden) silicone-based bandage (Fig. 4). The artificial pulmonary ventilation was done using the Mindray WATO EX-35 anesthesia machine (China) following the mode of pressure control ventilation (PCV).

The monitored vital parameters included the pulse-oximetry, the carbonometry, the electrocardiography (ECG), the non-invasive measurement of blood pressure and thermometry. The blood circulation parameters (blood pressure — non-invasive, heart rate, ECG) were controlled at all the stages of surgical intervention, as well as in 2 hours after surgery at the hospital ward. These parameters had stable values at all the stages. In order to prevent the skin damage when fixating the ECG electrodes and the peripheral venous catheter, the soft silicone-based patches were used (Mepitac, Sweden) (Fig. 5).

Under the cuff of non-invasive blood pressure measurement equipment, the Rolta-soft (Germany) synthetic cotton layer was placed. For preventing the skin damage, under all the areas of bony prominences, gel pads were placed for the whole surgical intervention.

The duration of surgical intervention was 195 minutes, the anesthesia lasted for 210 minutes. In order to observe the multimodal principle of post-operative analgesia, 30 minutes before the end of surgery, followed the intravenous administration of 30 mg Ketorol solution and 1000 mg of Paracetamol. In order to support the antiemetic effect of Dexamethasone and Metoclopramide (control of nausea and vomiting), to the end of surgery, additional administration of Ondansetron was conducted at a dosage of 4 mg (risk of post-operative nausea and vomiting in a patient when applying the Apfel scale is 3 points, or 60%). The extubation was carried out after the complete re-gaining of consciousness and of the neuromuscular conductivity. After 2 hours in a specialized Department ward, additional evaluation of the post-operative nausea was performed with the detailing of the patient's subjective sense of foreign body presence, coughing and difficulties while breathing after removing the endotracheal tube.

The post-operative period had a favorable course without complications. No complaints regarding the status of the upper airways and the oropharynx after the extubation were reported by the female patient. No episodes of post-operative nausea or vomiting were registered at the early post-surgery period. The female patient has noted a significant improvement in her ability to shut the eyelids with a background of complete survival of the transplants in the lower eyelids.

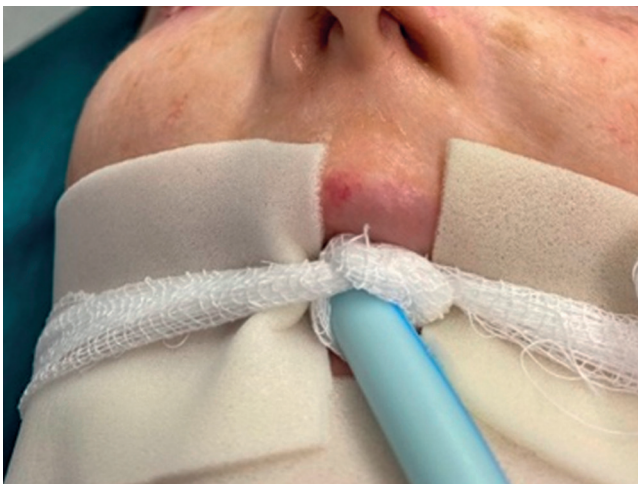

Fig. 4. The method of protecting the skin during the fixation of endotracheal tube using non-adhesive silicone dressings.

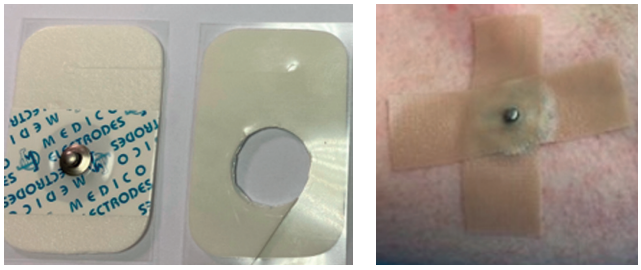

Fig. 5. The method of fixating the electrodes for ECG-monitoring with silicone patches with the adhesive part removed.

Restoring the functions of nasal breathing, of the visual organs and the elimination of dysphagia using the method of endoscopic balloon dilation has allowed for discharging the female patient on day 8 after surgery in generally satisfactory status for further out-patient treatment.

Eleven months after surgery, during the repeated visual examination and general check-up, no signs of recurrence of the eliminated complications of the main disease were detected in the patient.

DISCUSSION

The most frequent non-dermal manifestations of the Kindler syndrome are the damage of the gastrointestinal tract, of the urogenital system and of

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the visual organs. The national and foreign scientific literature has insufficient data on the selection of anesthesia method and on the perioperative managing of this category of patients. Besides, there are no data found on arranging the simultaneous surgeries in the settings of general anesthesia in Kindler syndrome patients in the accessible literature sources. Currently, a certain experience was gathered on selecting the anesthesia in case of surgical treatment among the patients with other types of epidermolysis bullosa, which, generally, depends on the severity of the main disease, as well as on the extent and the duration of surgical intervention. According to the literature data, in patients with epidermolysis bullosa, the methods that can be safely used include the general anesthesia, the neuraxial and the regional types of anesthesia [4]. During the period of preparing the patient for surgery, just like at the stage of its completion, it is important to keep in mind the necessity of preserving the patient's ability for unassisted relocation to the surgery table, due to which the preanesthetic medication in adult patients is generally not used [5].

According to the data from S.L. Solanki et al. [5], general anesthesia is the method of choice in patients with Kindler syndrome. At the same time, we suggest it is important to keep in mind that this type of anesthesia in such patients is associated with traumatic manipulations (direct laryngoscopy, videolaryngoscopy, mask ventilation) and risks of developing large bubbles in the laryngeal part of throat when using the devices intended for assuring the passability of the airways (air lines, endotracheal tubes). According to the opinion from B.Z. Mello et al. [6], when using the lubricants with abundant lubing the laryngoscope blade and the endotracheal tube, the risk of bubble formation significantly decreases.

Taking into consideration that Kindler syndrome patients are related to the category of patients with difficult airways, the conduction of combined general anesthesia with tracheal intubation remains quite a difficult task even for the experienced anesthesiology and resuscitation physicians, also due to the possible necessity of emergency use of surgical methods for restoring the passability of the upper airways (tracheostomy, cricothyrotomy) in case of bubbles forming with the development of asphyxia [7]. The issue of using supraglottic air tubes until the present moment remains disputable, for even the minimal traumatization during this procedure can contribute to the formation of bubbles in the mucosal membrane of the laryngopharynx [7]. Besides, there are insufficient data on selecting the devices and on the practical features of using the supraglottic air tubes in patients with epidermolysis bullosa [4].

Tracheal intubation, as the most reliable method of protecting the upper airways, especially in the presence of dysphagia, from our point of view, is the method of choice when arranging the anesthesia in this category of patients. In cases of single-level lesions in the esophagus, the balloon dilation can be carried out in the settings of intravenous anesthesia, without the tracheal intubation [8], while in cases of multi-level lesions — only in the settings of general anesthesia with the intubation of trachea.

In the presented clinical case, we have demonstrated the successful usage of video-assisted tracheal intubation with the background of microstomia in a Kindler syndrome patient, however, care should be taken regarding the possibilities of successful usage of fiber optic methods in such patients [5]. Sadly, but, according to our own experience of treating the patients with congenital epidermolysis bullosa, as well as according the experience of the foreign colleagues, it is not always possible to perform the endotracheal intubation using fiber optic techniques, for some cases require combining it with videolaryngoscopy [9].

In all the patients with congenital epidermolysis bullosa, regardless of the type of diseases, there are high risks of perioperative complications related to the intra-operative monitoring of vital functions, such as damaging the skin or mucosa when conducting the ECG monitoring, pulse oximetry, non-invasive measurement of blood pressure, providing the temporary vascular access (catheterization of the peripheral and central veins). There is no doubt that the major importance in the work of an anesthesiologist-intensivist managing such patients belongs to the use of medical products based on silicone without the adhesive components, not leading to iatrogenic damage of the skin or mucosal membranes.

CONCLUSION

The presented clinical case demonstrates the possibility of safely performing the simultaneous surgery in patients with congenital epidermolysis bullosa. The issue of the extent of surgical intervention will be defined for each patient on an individual basis. Protecting the skin and the mucosal membranes when arranging the anesthetic support in Kindler syndrome patients is the fundamental principle that allows for avoiding complications.

The development of modern medical technologies with using the microsurgical and endoscopic methods, the usage of personalized approach in selecting the anesthetic support allow for wider application of simultaneous surgeries in the treatment of complications in patients with Kindler syndrome.

ADDITIONAL INFORMATION

Author contributions: *V.I. Kornev*, *V.M. Machs*, *A.S. Pleshkov*, conducting the anesthesia and surgical treatment of the patient; *V.I. Kornev*, *M.V. Nikiforov*, consulting and examining the patient; *V.I. Kornev*, analyzing the treatment results, supervising the treatment and discussing the treatment results, compiling the article text. Thereby, all authors provided approval of the version to be published and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Consent for publication: The authors received written informed voluntary consent from the patient to publish her personal data, including photographs (with the face covered), in a scientific journal, including its electronic version (signed on 02.08.2024). The amount of published data is agreed with the patient.

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