



Ehlers-Danlos Syndrome Type IV – Anaesthetic Considerations

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Abstract

Ehlers-Danlos syndrome (EDS) is a rare disorder that occurs due to genetic defect in the collagen synthesis. The vascular subtype of EDS (type IV) is defined by characteristic facial features, translucent skin, easy bruising, and spontaneous arterial rupture and visceral perforation of such organs as the uterus and intestines, with possible life-threatening consequences. We report a case of a 15-year-old male patient with no past medical history undergoing emergency laparotomy after a spontaneous sigmoid colon perforation. Post-operatively and during the ICU stay complications developed and several revision operations and invasive procedures were necessary. A chest CT angiography revealed a right subclavian artery aneurysm, which was treated by an endovascular stent grafting. Taking into consideration the family history and clinical presentation EDS type IV was discussed as a possible cause of the patient's condition. DNA analysis confirmed the diagnosis. Due to the lack of evidence-based recommendations the anaesthetic management of these patients is still challenging.

Keywords

anaesthesia, complications, connective tissue, rare disease

INTRODUCTION

Ehlers-Danlos Syndrome (EDS) is a heterogeneous group of hereditary connective tissue disorders caused by a genetic defect in collagen synthesis that affects many organ systems.¹ According to the latest classification, there are 13 different manifestations of the syndrome, 12 of which are connected to genetic defects, either with autosomal dominant or autosomal recessive inheritance.² The clinical features of EDS vary in their severity and include skin fragility, joint hypermobility, and spontaneous rupture of blood vessels and internal organs.

CASE REPORT

A 15-year-old male patient with no past medical history presented with lower abdominal pain and vomiting. On clinical

examination, pale skin and bilateral clubfeet were noted. Family history revealed that his mother had died of peritonitis after multiple spontaneous intestinal perforations at the age of 22 years. No diagnosis had been made.

Emergency laparotomy under general anaesthesia revealed a spontaneous sigmoid colon perforation. Segmental resection with immediate re-establishment of continuity of the bowel was performed. Postoperatively, the patient was monitored uneventfully for two hours in the recovery room and then transferred to a surgical ward.

Six days later the patient developed wound dehiscence and clinical signs of peritonitis. After emergency surgery, the patient was admitted to the ICU with sepsis: temperature 38.7°C, tachypnea > 33/min, PaO₂/FiO₂=283, MAP 73 mm Hg, HR 140/min. A SOFA score progression from 0 to 2 over the previous six days was recorded. All haematological laboratory testing on admission to the ICU was normal. During the 44 days of ICU stay three revision operations because of

leakage from the anastomosis were necessary. In addition, bilateral pleural effusions developed requiring bilateral thoracocentesis and thoracostomy. A chest CT scan suggested a right subclavian artery aneurysm which was proven by chest CT angiography (Fig. 1). A decision was made for the patient to undergo endovascular stent grafting.

During the procedure, right brachial artery access was undertaken. The patient remained stable and lightly sedated with midazolam i.v. and fentanyl i.v. at a Ramsey Sedation Scale of 2. The following day, clopidogrel 75 mg p.o. and aspirin 100 mg p.o. were started. Two days later, bleeding from the abdominal operation site occurred with the need for further surgical revision. After consultation with the cardiologist who performed the endovascular procedure, aspirin administration was discontinued. On the fifth day after the stent grafting a huge soft tissue haematoma on the right upper arm ruptured spontaneously and massive haemorrhage ensued. Anaemia with Hb = 6.2 g dL⁻¹ and Hct 0.18 was recorded. Blood coagulation tests revealed INR 1.27, plasma fibrinogen 4.88 g l⁻¹ (normal range = 2.0 – 4.0 g l⁻¹), platelet count and clotting factors II, VII, VIII, IX, X within the normal range. Endotracheal intubation and mechanical ventilation were instituted, and a norepinephrine infusion was started. Eight units of RBCs, 8 units of FFP and 5 units of platelet concentrates were transfused over a 12-hour period. Tranexamic acid (1 g i.v.) was administered. The haemorrhage was surgically controlled and the patient remained hemodynamically stable, without any further bleeding. Clopidogrel was stopped and replaced with enoxaparin 6000 IU s.c. daily. After 44 days in the ICU, he was discharged in good condition.

The family history and clinical presentation led to consideration of Ehlers-Danlos syndrome as a possible cause of the patient's condition. DNA analysis confirmed the diagnosis of EDS type IV, revealing a mutation in the COL3A1 gene, which leads to abnormal type III procollagen synthesis.

DISCUSSION

EDS type IV, also known as vascular EDS, is a rare disorder associated with spontaneous arterial rupture and visceral perforation of such organs as the uterus or intestines, and possible life-threatening consequences.³ Due to the lack of scientific information and evidence-based recommendations, the anaesthetic management of these patients especially from a haematological viewpoint is challenging. Vascular EDS features thin, easily bruised and translucent skin. Taking into consideration the fragility of the soft tissue and blood vessels, open and endovascular procedures are fraught with high complication rates.⁴ As the majority of these patients are prone to bruising and haematoma formation even from repetitive non-invasive blood pressure measurements, invasive monitoring and central venous catheterization should be avoided whenever possible.

Regarding airway management, repeated intubation attempts and large endotracheal tubes may increase the bleeding risk from mucosal damage. Tracheal tube cuff pressure should be maintained as low as possible. Because of the risk of pneumothorax, airway pressure should be minimized, especially during laparoscopic surgery.



Figure 1A

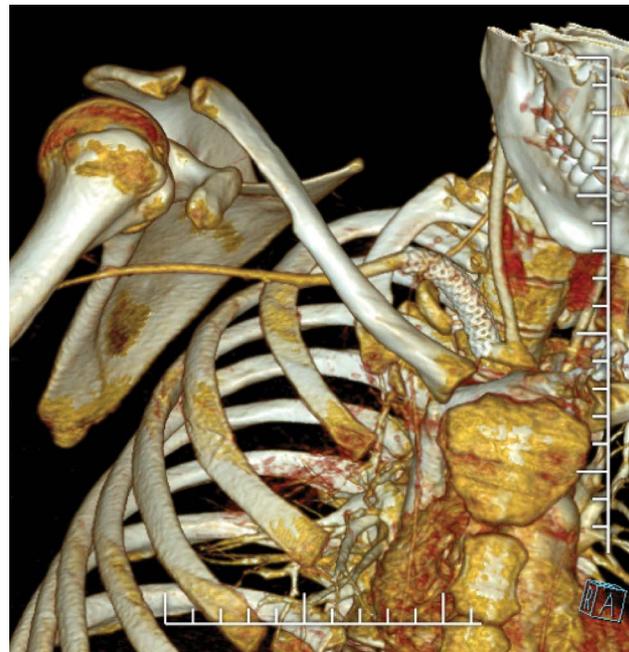


Figure 1B

Figure 1. CT angiography showing a highlighted right subclavian artery aneurysm before (1A) and after the endovascular stent grafting (1B).

Although haematological laboratory testing is usually within the normal range, platelet aggregation abnormalities occur in about 26% of patients.⁵ Autologous donation and prophylactic use of tranexamic acid should be considered.⁶ Desmopressin improves the bleeding time and reduces transfusion requirements by increasing plasma levels of Factor VIII and von Willebrand Factor. All these treatments should be considered preoperatively in vascular EDS.⁷ As EDS type IV is not associated with any alterations in drug pharmacokinetics and pharmacodynamics, balanced general anaesthesia is appropriate. All types of neuromuscular blocking drugs are safe to use. But it is recommended to avoid neuraxial blockade in patients with vascular EDS.⁴ Whenever possible intravenous patient-controlled analgesia should be used postoperatively.

We hope that future trials and evidence-based recommendations will identify the ideal strategy for the anaesthetic management of patients with EDS type IV. Anaesthesiologists should not underestimate the potentially life-threatening complications of this condition.

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Синдром Элерса-Данлоса, тип IV – анестезиологические соображения

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Резюме

Синдром Элерса-Данлоса (СЭД) – редкое заболевание, которое возникает из-за генетического дефекта синтеза коллагена. Судистый подтип СЭД (тип IV) характеризуется характерными чертами лица, полупрозрачной кожей, легко возникающими синяками, а также спонтанными разрывами артерий и внутренними перфорациями органов, таких как матка и кишечник, с опасными для жизни последствиями. Мы сообщаем о случае 15-летнего пациента без истории болезни, которому была выполнена экстренная лапаротомия после спонтанной перфорации сигмовидной кишки. В послеоперационном периоде и во время пребывания в отделении интенсивной терапии развились осложнения, потребовалось несколько ревизионных операций и инвазивных вмешательств. КТ-ангиография молочных желез выявила аневризму правой подключичной артерии, которая была обработана эндоваскулярным стент-графтом. Учитывая семейный анамнез и клинические проявления, СЭД типа IV обсуждалось как возможная причина состояния пациента. Анализ ДНК подтвердил диагноз. Из-за отсутствия рекомендаций, основанных на доказательствах, анестезиологическое обеспечение таких пациентов всё ещё остаётся проблемным вопросом.

Ключевые слова

анестезия, осложнения, соединительная ткань, редкое заболевание