Case Report / Приказ болесника

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Anesthesia for thyroid surgery in heart transplant patients – first case study in Serbia

Anestezija за операцију штитасте жлезде код пацијентана са трансплантираним срцем – приказ првог случаја у Србији

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Анестезија за операцију штитасте жлезде код пацијената са трансплантираним срцем – приказ првог случаја у Србији

SUMMARY
Introduction The number of patients in the world who have undergone heart transplantation is increasing, with better and longer survival rates, and therefore the number of patients who undergo various surgical interventions after transplantation is also increasing. This presents a challenge for anesthesiologists.

Case outline A 45-year-old female patient underwent a total thyroidectomy due to suspected thyroid cancer. She had a heart transplant three years earlier. Preoperative preparation included evaluation of cardiac function, consultative examinations by a transplant cardiologist, laboratory and other diagnostic procedures, as well as a detailed analysis of all 20 medications that the patient uses in daily therapy. Common drugs were used for premedication and general endotracheal anesthesia, with careful dose titration. Medicines were also prepared for the occurrence of heart rhythm disorders, bearing in mind that the heart is denervated, but there was no need for their use. The operation and postoperative course went smoothly and on the third postoperative day the patient was discharged from the hospital in good general condition.

Conclusion Preoperative preparation, anesthesia and postoperative treatment of this patient represented a challenge for our team, which was successfully overcome, considering that this is the first case of operative treatment of a patient with a transplanted heart in Serbia.

Keywords: thyroidectomy; transplanted heart; preoperative preparation

INTRODUCTION

Heart transplantation is the treatment of choice for decompensated heart failure that does not respond to conventional therapy, idiopathic dilated cardiomyopathy and terminal ischemic heart disease. [1, 2] Since 1967, when Christian Bernard performed the first heart transplantation, a large number of those operations have been performed and it is constantly increasing. Only in the USA over 3000 heart transplant operations are performed each year, while, according to the data of the International Society for Heart and Lung Transplantation in Europe, that number is around 1500–3000 annually [3]. Five-year survival rate after heart
transplantation is over 72.5%, and twenty-year survival is 21% [4]. Considering the increasing number of transplantations and life expectancy of those patients, the number of non-cardiac interventions performed on patients with previous heart transplantation is rising. In Serbia, the first heart transplant procedure was performed in 1995, when five patients were successfully operated. The Heart Transplant Program was revived in 2013, and so far 49 patients have been successfully operated at the University Clinical Centre of Serbia (UCCS). To the best of our knowledge, apart from our patient, none of the others, previously mentioned patients, have yet undergone any other post-transplantation surgery, which certainly represents a great challenge for us. Naturally, post-transplantation surgery requires the participation of the cardiologist involved in the post-transplantation monitoring program and an experienced team of anesthesiologists.

CASE REPORT

A female patient, 45 years old, was admitted to the Clinic for Endocrine Surgery (CES) UCCS for surgical treatment of the thyroid gland. In 2018 she underwent the heart transplantation procedure. Her heart problems began in 2005, when she received the seasonal flu vaccine, after which she developed a fever, malaise lasting for four weeks, along with fatigue, angina pectoris and dyspnea. Multiple chest X-rays were performed, as well as other examinations, but there were no signs of pneumonia nor cardiac decompensation. Her medical problems lasted for two and a half years, while she was being treated with antibiotics under suspicion of chronic bronchitis. After the mentioned period, episodes of angina pectoris and dyspnoea reappeared. Coronary disease was excluded by coronary angiogram examination. All branches of coronary arteries showed no significant stenosis in their proximal and distal parts.

An echo cardiogram revealed a pericardium filled with fluid, enlarged heart cavities, with severe reduction of left ventricular systolic function with ejection fraction of left ventricle (EF LV) 17%, which led to diagnosis of dilated cardiomyopathy. The next cardiac deterioration occurred in 2014 after a common cold, when she was treated conservatively, but due to her weakened heart and compromised hemodynamic, a pacemaker and defibrillator were implanted (ICD-VR). The heart transplantation was performed in 2018. Graft that was used was a healthy heart with normal anatomic characteristics and EF LV 65%. During operation pacemaker and defibrillator were removed, but their wires couldn’t be removed because one of them had fused with the vagal nerve, and the other one had been dislocated towards the right heart cavities
where it is still located (Figure 1). Short and long-term postoperative outcomes passed without any complications (in form graft rejection, infections, allograft vasculopathy and malignancy).

Regarding her commodities, our patient is obese (body weight = 99 kg, body height = 176 cm, body mass index = 32 kg/m²), has confirmed hyperlipidemia, arterial hypertension and mild pulmonary hypertension. Since last year, she has been treated for diabetes with intensive insulin therapy (short acting human insulin 6+8+8 IU before meals and intermediate acting human insulin 14 IU in the evening at 10 p.m.). She had COVID-19 on two occasions, once treated at home (in 2021) and the other time in a hospital (in 2022), both times with mild symptoms. She has not been vaccinated against the corona virus.

On June 22nd, 2022 she was admitted to CES UCCS for operative treatment of the thyroid gland. A neck echotomographic examination verified a node in the left lobe of the thyroid gland about 4.5 cm in size of iso- to heteroechoic characteristics with the presence of intranodal vascularization. Fine Needle Aspiration Biopsy was performed and the obtained sample was analyzed. The result indicated an atypia of undetermined significance – Bethesda system III, which established the probability of thyroid cancer. Laboratory analyses (blood count, biochemistry, coagulation status) performed on hospital admission day showed no significant deviations from the reference values. N-terminal pro-B-type Natriuretic Peptide (NT pro-BNP) was 68 pg/ml before operation. Electrocardiogram (ECG) showed the presence of a biphasic p-wave with rhythm of 82 beats per minute. Chest radiography did not show any presence of consolidations and X-ray of cervical spine indicated degenerative changes in the form of uncarthrosis and reduction of the C5-C6 intervertebral space. Echocardiogram revealed an accelerated flow through the aortic valve, paradoxical movement of interventricular septum, EF LV 70%, weaker longitudinal function of right ventricle, severe tricuspid regurgitation, an indirectly assessed elevated systolic pressure in the right ventricle and a wire visible in the right heart cavity.

Together with the transplant cardiologist who followed-up the patient after the transplantation, all 20 drugs that the patient uses on a daily basis were analyzed, in order to determine the optimal regimen, doses and timing for their application in the perioperative period, as well as possible interactions with medications that could be used during anesthesia (Table 1). She regularly took her therapy the day before surgery, and morning on the surgery day. Also, she received an antibiotic 1 hour before surgery (vancomycin 2 g intravenously), low molecular weight heparin (enoxaparin sodium 0.4 ml subcutaneously) 2 hours before surgery, gastro protective therapy (pantoprazole 20 mg orally), as well as her personal
cardiology therapy (ivabradine 7.5 mg orally) and therapy for the regulation of pulmonary hypertension (sildenafil 20 mg).

For premedication the patient received 5 mg of midazolam intramuscularly half an hour before surgery. During that period, she was under constant observation. In the meantime, in the operating room we prepared medications for possible intraoperative bradycardia (adrenaline in a dilution of 1:200 000) and tachycardia (amiodarone in a dilution of 1:4), as well as a defibrillator.

Non-invasive monitoring (ECG, pulse oximetry, NIBP, etCO$_2$, RR) was used intraoperatively. Before general endotracheal anaesthesia (GEA) induction, the patient was preoxygenated with 100% oxygen (flow 6 L/min) for 5 minutes. During preoxygenation, she received 25 mg of hydrocortisone intravenously, in order to prevent acute adrenal insufficiency, bearing in mind that she regularly used glucocorticoids (prednisone) after transplantation.

Propofol (160 mg) was used for GEA induction, rocuronium bromide in a dose of 0.8 mg/kg was used for intubation, and following muscle relaxation. The patient was intubated using a video laryngoscope (Glide-scope). To maintain anaesthesia, a gas mixture of sevoflurane (2 vol%), oxygen (50%) and air (50%) was used. For analgesia, diluted fentanyl (1:4) was used in intravenous bolus doses, starting before induction, up to a total dose of 150 mcg. Sugammadex was used to reverse the neuromuscular block in a dose of 4 mg/kg.

During the procedure hemodynamic parameters remained stable. Initial arterial tension (AT) was 123/74 mm Hg, and heart rate (HR) was 80/min. The highest measured value of AT was 130/75 mm Hg, and HR 80/min. The operation (total thyroidectomy) lasted 50 minutes and passed without any complications. The patient was extubated on the operating table, after all conditions were met (consciousness presence, performing all orders, adequate motor response, spontaneous respiration with frequency 12/min, oxygenation > 95%, hemodynamically stable). She was transferred to the Coronary Care Unit (CCU) for 24-hour monitoring by a cardiologists. In the CCU she received her own cardiac, immunosuppressive and other chronic therapy. The concentration of tacrolimus in blood was in the therapeutic range postoperatively. Postoperative value of NT pro-BNP was 75 pg/ml. The patient was transferred to the surgical ward 24 hours after the operation, and on the third postoperative day she was discharged from the hospital with therapy recommendation. Postoperative period passed without any complications. There were no arrhythmias detected during perioperative period.
This case report was approved by the institutional ethics committee, and written consent was obtained from the patient for the publication of the case report.

DISCUSSION

The number of heart transplantations worldwide is constantly rising; the success of this surgical procedure is greater with higher post-transplant survival rate, and experiences with non-cardiac surgeries of those patients are increasing [5]. However, here in Serbia we cannot claim that we have excessive numbers and experiences with such patients. According to our knowledge, this was the first case of a patient with previous heart transplant undergoing non-cardiac surgery, so the challenge for our anesthesia team was even greater.

Numerous physiological factors within previous heart transplant patients must be taken into account during preoperative preparation and GEA, such as denervation of transplanted heart, number and influence of other medications those patients use on a daily basis (like interaction between immunosuppressant and anesthetics), possibility of graft rejection, proper perioperative pain therapy and the possibility of infection [6].

After heart transplantation, the graft tissue has its own sinoatrial (SA) node, which is completely denervated and independent of the host’s autonomic nervous system, so in those patients we can expect the following: a lack of baroreceptor reflex, no response to carotid sinus massage, change in a heart frequency as a postural change and lack of reaction to Valsalva maneuvers [7, 8]. It is also known that after heart transplantation, due to vagal denervation and increased sensitivity of the graft myocardium to circulating catecholamines, episodes of arrhythmias and blockages (such as first-degree atrioventricular block) can occur, which are usually detected after the transplant surgery [9]. Having that in mind, the use of atropine in case of intraoperative bradycardia would not be effective, and use of beta-blockers in case of intraoperative tachycardia is not advised because of their wide range of cardiopulmonary effects and it can also cause potential total blockade of the heart muscle [10]. Considering these facts, our team was prepared to respond to potential rhythm changes with solutions of amiodarone and adrenaline. Some authors recommend verapamil for tachycardia and vasopressors (noradrenaline, dobutamine) for bradycardia treatment [11, 12].

Unlike in the non-heart transplant patients, reversing neuromuscular blockade with neostigmine and atropine in heart transplant patients remains a topic for further scientific research. It is also known, from the available scientific literature, that meta-analysis had been
performed and proved that a smaller number of adverse reactions occur when using sugammadex compared to anticholinesterase drugs, therefore we decided to reverse neuromuscular block using sugammadex [3].

Signs of graft rejection must always be ruled out preoperatively, because scientific evidence showed that patients who undergo a surgical procedure and have proven indicators of graft rejection have a higher morbidity compared to those in whom rejection is excluded [13]. For these reasons, a heart muscle biopsy was performed preoperatively in our patient to rule out signs of rejection reaction.

It is better to avoid invasive procedures whenever possible because the risks of various complications (including infection) outweigh the benefits that invasive monitoring can provide, so we decided to use non-invasive monitoring because we assessed that it was an operation with low intraoperative risk and that the patient was stable in terms of comorbidities thus reducing the risk of infection [14]. This proved to be a good strategy because the patient was hemodynamically stable throughout the whole operation.

To conclude: the patient who had a heart transplant four years earlier underwent total thyroidectomy under suspicion of thyroid cancer under general endotracheal anesthesia. In cooperation with the transplant cardiologist, she was well pre-operatively prepared for the operation. She tolerated the operation and GEA well and was discharged from the hospital on the third postoperative day in good condition. This is the first case of operative treatment of a patient with a transplanted heart in Serbia.

**Conflict of interest:** None declared.
REFERENCES


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Figure 1. Patient’s chest X-ray
### Table 1. Drugs, doses, and timing of their use

<table>
<thead>
<tr>
<th>Drug name</th>
<th>Drug group</th>
<th>Drug dose</th>
<th>Timing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Furosemide</td>
<td>Diuretic</td>
<td>40 mg</td>
<td>8 a.m.; 6 p.m.</td>
</tr>
<tr>
<td>Amlodipine</td>
<td>Antihypertensive</td>
<td>2.5-5 mg</td>
<td>12 p.m.</td>
</tr>
<tr>
<td>Sildenafil</td>
<td>Antihypertensive</td>
<td>20 mg</td>
<td>8 a.m.; 4 p.m.; 00 a.m.</td>
</tr>
<tr>
<td>Ivabradine</td>
<td>Antiarrhythmic</td>
<td>5 mg</td>
<td>8:15 a.m.</td>
</tr>
<tr>
<td>Human insulin*</td>
<td>Antidiabetic</td>
<td>6+8+8 IU</td>
<td>before meals</td>
</tr>
<tr>
<td>Human insulin**</td>
<td>Antidiabetic</td>
<td>14 IU</td>
<td>10 p.m.</td>
</tr>
<tr>
<td>Prednisone</td>
<td>Corticosteroid</td>
<td>5 mg</td>
<td>8:15 a.m.</td>
</tr>
<tr>
<td>Mycophenolic acid</td>
<td>Immunosuppressant</td>
<td>1000 mg</td>
<td>10 a.m.; 10 p.m.</td>
</tr>
<tr>
<td>Tacrolimus</td>
<td>Immunosuppressant</td>
<td>3 mg</td>
<td>10 a.m.; 10 p.m.</td>
</tr>
<tr>
<td>Rosuvastatin</td>
<td>Statin</td>
<td>10 mg</td>
<td>10 p.m.</td>
</tr>
<tr>
<td>Trimethoprim-sulfamethoxazole</td>
<td>Antibiotic</td>
<td>800/160 mg</td>
<td>Tuesday, Thursday and Sunday at 10:00 a.m.</td>
</tr>
<tr>
<td>Pantoprazole</td>
<td>Gastro Protection</td>
<td>40 mg</td>
<td>7:30 a.m.; 7:30 p.m.</td>
</tr>
<tr>
<td>Bromazepam</td>
<td>Anxiolytic</td>
<td>1.5-3 mg</td>
<td>optionally</td>
</tr>
<tr>
<td>Potassium chloride</td>
<td>Supplement</td>
<td>1 bag, each 3rs day 2 bags</td>
<td>9 a.m.</td>
</tr>
<tr>
<td>Calcium carbonate</td>
<td>Supplement</td>
<td>1000 mg</td>
<td>8:30 a.m.</td>
</tr>
<tr>
<td>Vitamin C</td>
<td>Supplement</td>
<td>1000 mg</td>
<td>9 a.m.</td>
</tr>
<tr>
<td>Vitamin D3</td>
<td>Supplement</td>
<td>2000 IU</td>
<td>8 p.m.</td>
</tr>
<tr>
<td>Folic acid</td>
<td>Supplement</td>
<td>5 mg</td>
<td>10 a.m.</td>
</tr>
<tr>
<td>Iron</td>
<td>Supplement</td>
<td>1000 mg</td>
<td>7:30 a.m.</td>
</tr>
<tr>
<td>Magnesium</td>
<td>Supplement</td>
<td>375 mg</td>
<td>8:15 a.m.; 8:15 p.m.</td>
</tr>
</tbody>
</table>

*short-acting; 
**intermediate acting