CASE REPORTS

Anaesthesia for Vaginal Prolapse Surgery in the Heart Transplant Recipient. A Case Report

Saimir KUCI^{1*}, Adriana MISJA¹, Alfred IBRAHIMI¹, Ermal LIKAJ², Petrit REXHEPI³, Orion GLIOZHENI³, Ilir OHRI¹

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Abstract

Introduction: Nowadays, we need to deal with heart transplanted patients for other medical concerns. So, it is important to see in detail different aspects and modalities of their care during other types of surgery. A transplant team will carefully monitor each heart trans-plant recipient and should be possible to seek information on the patient's overall status. They will be able to inform on the most recent investigations (ECG to assess graft function, recent biopsy for rejection, angiography for coronaries, etc.).

Case report: Our patient, a 65-year-old lady underwent heart transplantation 5 years before. The cardiac situation was stable and she was doing fine. She was recovered in the gynaecological clinic with a diagnosis of vaginal prolapse with surgical indication General anaesthesia was done with fentanyl 7 ml, pavulon 4 mg, propofol 200 mg and sevoflurane 1.5-2.2%. The patient was monitored during surgery with SpO2, ECG, IBP, CVP. The operation technique was open of vaginal plastic repair.

Discussion: By 3 months, most recipients of heart transplant came under New York Heart Association (NYHA) I class. The last UK national survey about health-related quality of life after cardiac transplantation indicates that, 1 year after surgery, there is an improvement in quality of life (60% are much better; 28% somewhat better) and there is no deterioration in general health at 3–5 years, except that many of them have symptoms compatible with depression.

Conclusion: Perioperative care of heart transplant recipients will entail a greater attention to maintaining an adequate preload and vascular tone, to avoiding infections and to being aware of the multiple side effects of immunosuppressive therapy. References and recommended reading

Papers of particular interest, published within the annual period of review, have been highlighted as: of special interest of outstanding interest Additional references related to this topic can also be found in the Current World Literature section in this issue

Keywords: Heart trasplant, denervated organ, immunosuppressants

Introduction

The patient with heart transplant can be managed as any other patient, and a careless anaesthetist could cause great harm by doing so; however, the days when these patients were handled exclusively by specialized teams are long gone.

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* Corresponding author: Saimir KUÇI MD, PhD saimirkuci@gmail.com

1 Department of Anaesthesiology University Hospital Centre "Mother Teresa" Tirana, ALBANIA

2 Department of Cardiac Surgery, University Hospital Centre "Mother Teresa" Tirana, ALBANIA

3 Department of Obstetrics and Gynecology "Koco Gliozheni" Hospital, Tirana, ALBANIA These patients often require the expertise of nontransplant specialists when they present with new health problems, sometimes many years after their transplant.

Anaesthetists need to remain abreast of new developments in the field of cardiac transplantation. Discussing the patient with the transplant team in advance of potential surgery will help minimize problems in the perioperative period.

Physiology of the transplanted heart

The transplanted heart is a denervated organ, but intrinsic cardiac mechanisms are preserved and the heart will be exquisitely sensitive to changes in filling conditions, and the Starling volume–pressure relationship becomes paramount in adjusting contractility.

The resting heart rate is high (90 - 100 bpm) as vagal tone is lost. Tachycardia in response to physiological stress (such as hypovolaemia) is blunted as it depends on



circulating hormones. Atropine or glycopyrrolate do not have their usual effect [1.2]. With time, some degree of functional reinnervation is reestablished. Scientific evidence in the form of trials looking at catecholamine uptake and heart rate variability support these clinical observations [3]. Occasionally, other mechanisms can mimic reinnervation, perhaps giving a sense of false security.

Heart transplant patients will present with a higher rate of cardiac dysrhythmias due to the absence of vagal tone, coupled with conduction abnormalities. First-degree atrioventricular block is common, and up to 30% of patients have right bundle branch block. About 5% of patients will need a permanent pacemaker in the early postoperative period [5].

Complications following transplantation

Survival after cardiac transplantation is now above 90% at 1 year and around 50% at 10 years [6]. Longer survival allows other ailments to develop in these patients and around a third of all heart transplant recipients will require noncardiac surgery [7], with a high incidence of malignant disease [8]. Patients' natural history will continue to progress, and the burden of old age comes alongside the complications related to the required immunosuppression. It is noteworthy that more than 50% of heart transplant recipients are 50 years old or over at the time of transplant.

Apart from rejection and infection, the heart recipient patient is more likely to have diabetes, epilepsy and hypertension (all as a result of drugs used to prevent rejection). These patients have a higher incidence of cholelithiasis and pancreatitis. Preeclampsia is a risk for female recipients who become pregnant. With the passage of time, patients will progressively develop chronic allograft vasculopathy, an immune-mediated disease.

Rejection

The balance between too much immunosuppression (with a risk of infection) or too little (with a risk of rejection) is difficult to achieve. Up to 40% of heart transplant recipients have an episode of acute rejection requiring treatment during the first year. Acute rejection is infrequent after the first year, but can occur if patients do not take immunosuppressants regularly or if several doses are omitted while they are in hospital for noncardiac illness.

Diagnosis

Bradycardia, atrial fibrillation or flutter, fatigue, fever, unexplained weight gain, peripheral oedema and dyspnoea should prompt investigation with an endomyocardial biopsy to confirm a diagnosis of acute rejection. Biopsies are graded according to the guidelines described by the International Society for Heart and Lung Transplantation. A negative biopsy does not exclude a rejection [9]. The amount of endocardial infiltration by lymphocytes might be correlated with outcome [10,11].

Less of the sinoatrial node can lead to bradycardia and hypotension, as observed after administration of invasive diagnostic methods are being investigated, such as detecting modifications in gene expression patterns. These might allow earlier detection as well.

Prevention

Immunosuppression is the cornerstone of prevention of rejection. Novel strategies using peptides with antiinflammatory and antioxidant properties, such as statins, apolipoproteins and omega-3 fatty acids, may also contribute [12,13,14].

Surveillance biopsies are carried out regularly (usually through the right internal jugular vein).

An association between an elevated brain natriuretic peptide (BNP) concentration and molecular patterns of active cardiac structural remodelling, vascular injury, inflammation and allo immune processes is described in the clinically quiescent phase after cardiac transplantation [15] and has been investigated as a marker of rejection; however, so far it has no clinical usefulness.

Treatment

Episodes of acute rejection require increased immune suppression; for antibody-mediated rejection, intravenous (i.v.) immunoglobulins and plasmapheresis are sometimes used. Very rarely patients may need mechanical support till cardiac function recovers following a severe episode.

A special case: cardiac allograft vasculopathy

Cardiac allograft vasculopathy (CAV) is the leading late cause of death after heart transplantation. Intravascular ultrasound (IVUS) is the most sensitive technique to detect early changes, and increased intimal thickening at 1 year has been shown to be a marker of early CAV. Aetiology is complex but includes both immunological and nonimmunological factors (hyperlipidaemia and hypertension) [16].

Angioplasty with drug eluting stents is used when focal, proximal lesions are detected, but new lesions distal to the site of intervention are frequently seen [17].

Disease is often widespread; and distal revascularization by any method is impossible. It is important to maintain adequate coronary perfusion pressure during anaesthesia.

Infection

Is a common problem in the early postoperative period in patients who need a prolonged stay in the ICU. Acute renal dysfunction and postoperative bleeding are other common problems [8].

Infection is a predictor of poor outcome and accounts for up to 20% of deaths in the early posttransplant period [18,19].



Immunosuppression can delay wound healing and some drugs (e.g. sirolimus) have been associated with higher risk of wound infection [20].

Strict aseptic technique is mandatory when handling immunosuppressed patients. The number of indwelling catheters must be kept to a minimum and all invasive devices removed at the earliest opportunity.

Potential infections must be investigated with cultures before treatment is commenced and the possibility of opportunistic infections should be kept in mind. Fungal infection (Aspergillus and Candida) may require prolonged treatment. Cytomegalovirus (CMV) was the commonest opportunistic infection, but prophylaxis with valganciclovir has proved very effective. CMV negative blood must be used in all CMV negative patients. Pneumocystis carinii and Toxoplasma are rare infections that may present in the intensive care setting. Microbiology advice should be sought early in the course of the disease.

Immunosuppression Drugs

Leucodepleting agents may be used in the perioperative period and include antithymocyte globulin and the T-cell depleting agent OKT3. Interleukin (IL)-2 receptor antagonists (**basiliximab and dacluzimab**) are also used in the perioperative period.

Maintenance immunosuppressive regimes are based on a combination of three agents [21]: steroids (prednisolone), calcineurin inhibitors to suppress the production of IL-2 (ciclosporin or tacrolimus) and antiproliferative agents (azathioprine or mycophenolate mofetil). Proliferation signal inhibitors [also called mammalian target of rapamycin (mTOR inhibitors)] are increasingly been used, examples being sirolimus and everolimus.

Ciclosporin has been widely used for over 25 years and changed the face of transplantation when introduced. It is highly lipophilic and has variable bioavailability dosage is guided by blood concentration. A change in liver function will greatly alter ciclosporin concentrations. One-third of the oral dose can be given i.v. over 2 - 6 h. Ciclosporin interacts with many drugs, particularly agents that affect the cytochrome p450 system. It can lower seizure threshold in those patients with an underlying predisposition.

Renal impairment is a consequence of ciclosporin use and is one of the most important threats to the long-term success of transplantation, with a great impact on quality of life. Thirty per cent of patients will develop some degree of renal dysfunction in the first-year post transplant and up to 5 - 8% of heart recipients will eventually require renal replacement therapy, dialysis or kidney transplantation [22].

Proliferation signal inhibitors are not nephrotoxics per se, but can enhance the renal toxicity of calcineurin inhibitors.

Renal failure will affect the choice of anaesthetic drugs, either because they could be affected by impaired clearance or because they adversely affect the renal function. Other side effects of the classical regimen include hypertension (up to 76%), bone marrow suppression, hyperlipidaemia, all the side effects of steroids, hyperglycaemia (especially with tacrolimus and steroid), osteoporosis (higher risk of compression fractures), malignancy (causing up to 23% of deaths in patients after heart transplantation) and gastrointestinal disorders.

In an attempt to curtail these side effects without jeopardizing efficacy, various new regimens are being inves tigated. Some attempt to decrease the exposure to steroid by either avoiding them [23] or giving them for shorter duration, with perhaps an increased incidence of acute rejection [24].

Calcineurin inhibitor free regimes are now being investigated in order to minimize renal dysfunction. More recently, agents that inhibit the transduction of the proliferation signal after cytokines are combined with their receptors have been introduced in clinical practice. These newer agents are thought not to be nephrotoxic, have a lower incidence of malignancy [25] and may delay the onset of CAV. They have been reported to delay wound healing, and sirolimus is associated with inter- stitial pneumonitis [21].

A lymphocyte depleting mono- clonal antibody specific for CD52 on humans (alemtuzumab) has been shown to be efficient in treating patients with recurrent steroid resistant rejection episodes [26,27].

A better understanding of changes occurring with age now allows the dose of immunosuppressants to be reduced in older patients [28].

All these agents, old and new, can interact with drugs used during anaesthesia.

On the one hand, ciclosporin enhances the effect of nondepolarizing muscle relaxants such as vecuronium and pancuronium [29]

Azathioprine decreases the effect of nondepolarizing muscle relaxants [5].

Case presentation

Our patient, a 65-year-old lady underwent heart transplantation 5 years before. The cardiac situation was stable and she was doing fine. She was recovered in the gynaecological clinic with a diagnosis of vaginal prolapse with surgical indication.

Her maintenance therapy was cardiocor 1.25mg/d, sandimun 50 mg/d, ciclosporin (certican) 0.25 mg/d, prednisolon 50 mg/d.

Echocardiography revealed a normal functioning left ventricle with slight hypertrophy and relaxation disturbances. The left atrium was dilated to 23 cm2 with minimal mitral regurgitation. Normal aortic and tricuspid valve.

Laboratory data showed anaemia with a haemoglobin level of 7.8 g/l and erythrocyte count of 3.560.000. The rest was within normal limits. The chest x-ray and abdominal echography were normal.



In the preoperative period the patient was treated with liquid infusions, fresh blood, antibiotics and low molecular weight anticoagulants. The operative risk was determined as 2 according to ASA.

General anaesthesia was done with fentanyl 7 ml, pavulon 4 mg, propofol 200 mg and sevoflurane 1.5-2.2%. The patient was monitored during surgery with Spo2, ECG, IBP, CVP and urinary cathether. During surgery the patient received 1.5 1 NaCl 0.9 % solution and one unit of blood, heparine5000 UI, furosemide10 mg, dexamethasone 8 mg and NaHCO3 30 ml.

The anaesthesia was uneventfull, surgery was 120 min long and awakening was very good. The operation technique was open of vaginal plastic repaire. The patient had haemodymanic stability with a blood pressure of 130-110/70-80 mmHg and heart rate of 68 per min in sinus rythm. No inotropes and vasotonics were necessary. The patient was extubated without problems in the operatin room.

Postoperatively the patient received antiobiotics, anticoagulation and gastroprotective therapy apart from the usual immunosuppressive therapy. Rehabilitation was very fast without any cardiac disturbances.

Discussion

By 3 months, most recipients of heart transplant came under New York Heart Association (NYHA) I class. The last UK national survey about health-related quality of life after cardiac transplantation indicates that, 1 year after surgery, there is an improvement in quality of life (60% are much better; 28% somewhat better) and there is no deterioration in general health at

3–5 years, except that many of them have symptoms compatible with depression [30].

Preoperative assessment

A preoperative ECG is required, and continuous monitoring of the electrical activity is mandatory during the operation and in recovery. Two P waves may be seen; one from the remnant recipient atrium that is not conducted (as it is interrupted at the level of the suture line). Up to 5% of heart recipients will present with a pace- maker requiring the same attention as in other patients. Echocardiography helps to assess the left and right ven- tricular function [31]. Laboratory tests will include measures of renal function including principal electrolytes, inflammatory markers, coagulation and a full blood cell count to ensure the absence of bone marrow suppression [29]. Some advocate measuring the brain natriuretic peptide in heart transplant recipients. This peptide is stored in ventricular myocytes and released with increased trans- mural pressure. Several studies have demonstrated its relationship with chronic cardiac failure, but not in heart recipients in whom it remains high [32]. BNP may have a role in the detection of allograft rejection and coronary vasculopathy, but there is uncertainty whether

it affects prognosis [33–35]. If ciclosporin cannot be administered enterally after surgery, the i.v. dose is a third to a quarter of the oral dose. Therapeutic drug monitoring, attention to renal function and liaison with the transplant team will help to minimize toxicity.

Intraoperative management, anaesthetic technique

Premedication should be given as usual and if required [29]. The anaesthetic technique can be chosen according to the surgical needs. Both general and loco-regional anaesthesia can be performed as long as great care is given to maintain the preload [5]. No technique has been demonstrated to be better, but common sense must prevail and an epidural might allow better control of vascular tone than a subarachnoid block. Intraoperative management, airway management and ventilation. Oral intubation is preferred to nasal, because of the potential risk of infection caused by nasal flora [5,29].

Ciclosporin leads to gingival hyperplasia, and there is a greater amount of bleeding during airway manipulation. Difficulty in airway management can occur as a result of diabetes and lymphoproliferative disorders that cause obstructions. There is, however, no formal contra-indication to the use of a laryngeal mask. Hyperventilation should be avoided because ciclosporin and tacrolimus diminish the seizure threshold. A muscle relaxant such as cisatracurium is adequate, as its elimination is not affected by either renal or liver dysfunction.

Intraoperative management, haemodynamic control

If large fluid shifts are expected, further monitoring is indicated and this might include the use of a Swan - Ganz catheter. Noninvasive methods to measure cardiac output might be useful, and transoesophageal echocardiography is definitely a tool to consider. Drugs with direct pressor or chronotropic effects are required and isoproterenol, ephedrine or metaraminol, and adrenaline should be readily available. Amiodarone or verapamil will be useful in case of tachyarrhythmia. Levosimendan, a calcium sensitizer, which can increase cardiac contractility without changing calcium intracellular levels, may improve ejection fraction in heart trans- plant recipients when administered as a 24h infusion without bolus dose [36,37]. Beta-blockers should be avoided and caution applied when administering nitroglycerin or nitroprusside. Positioning is the key in those patients who have a frail musculo skeletal structure. Patients on long-term steroids may need intraoperative administration.

Postoperative care

Postoperative care is similar to the care given to nontransplanted patients, with perhaps enhanced attention



to preload, renal function, infection and coagulation. Thromboprophylaxis will be administered because of a high risk of deep venous thrombosis in the patients [29]. Immunosuppression must be continued and monitored [37].

Conclusion

Perioperative care of heart transplant recipients will entail a greater attention to maintaining an adequate preload and vascular tone, to avoiding infections and to being aware of the multiple side effects of immunosuppressive therapy. References and recommended reading

Papers of particular interest, published within the annual period of review, have been highlighted as:of special interest of outstanding interest

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