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Case Report

Bipolar disorder and heart transplantation: A case report[☆]



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ABSTRACT

Introduction: Bipolar disorder is a chronic and recurrent mood disease that includes symptoms that fluctuate from euphoria to depression. As a mood disorder, it is one of the main contraindications for transplantation procedures. The case is presented of a patient with bipolar disorder who had a heart transplant after a cardiac arrest. Heart transplantation is the treatment of choice in patients with heart failure and arrhythmias that do not respond to conventional treatment.

Methods: Case report and narrative review of literature.

Case report: A 34-year-old woman with bipolar disorder diagnosed when she was 13, treated with lithium and aripiprazole. She required a heart transplant as the only therapeutic option, after presenting with ventricular tachycardia refractory to conventional treatment. The patient did not suffer an emotional decompensation with the removal of the lithium and aripiprazole that were associated with prolonged QTc interval, and remained euthymic throughout the process.

Discussion: Heart transplantation can be performed safely and successfully in patients with bipolar disorder, when suitably followed-up by a liaison psychiatry group.

Conclusions: Bipolar disorder should not be considered as an absolute contraindication for heart transplantation.

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Trasplante cardiaco en paciente bipolar: reporte de caso

R E S U M E N

Palabras clave:

Trastorno bipolar
Taquicardia ventricular
Trasplante de corazón
Psiquiatría

Introducción: El trastorno bipolar es una afección del estado de ánimo, crónico y recurrente, que cursa con síntomas que fluctúan entre la euforia y la depresión. El trasplante cardiaco es el tratamiento de elección para pacientes con insuficiencia cardiaca y arritmias que no responden al tratamiento convencional, pero este tipo de procedimiento está contraindicado de manera absoluta o relativa para pacientes con trastorno bipolar.

Métodos: Reporte de caso y revisión narrativa de la literatura.

Caso: Mujer de 34 años con trastorno bipolar desde los 13, en tratamiento con litio y aripiprazol, que requirió un trasplante cardiaco como opción terapéutica por taquicardia ventricular refractaria al tratamiento convencional. La paciente no sufrió descompensación afectiva al retirársele el litio y el aripiprazol, que se debió suspender porque se asociaron con prolongación del intervalo QTc, y permaneció eutímica a lo largo del proceso con ácido valproico y clonazepam.

Conclusiones: Este reporte de caso muestra un trasplante cardiaco exitoso en una paciente con trastorno afectivo bipolar en eutimia y sin otras contraindicaciones psicosociales para el injerto. Además, destaca la importancia del seguimiento por psiquiatría de enlace durante el proceso.

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Introduction

Bipolar disorder is a chronic, recurrent mood disorder that includes symptoms that swing from euphoria to depression. It affects both males and females with onset between the ages of 20 and 30.¹ It affects 2–3% of the world population, making it more common than other medical diseases such as type 1 diabetes mellitus, rheumatoid arthritis and human immunodeficiency virus infection. Recent studies have shown that bipolar disorder is the sixth leading cause of disability in the world and it is associated with high morbidity and mortality rates. There are two types of bipolar disorder: type I, characterised by episodes of mania and depression; and type II, characterised by episodes of hypomania and depression²; type I has a prevalence of 1.3% in Colombia and type II, 0.2%.³

Ventricular tachycardia is common in patients with structural heart disease and is associated with sudden death. In general, treatment is curative using antiarrhythmic drugs, ablation therapy or implant of cardioverter defibrillators. In some refractory cases, heart transplantation may be necessary.⁴

Cardiac transplantation is the treatment of choice for patients with heart failure and arrhythmias who do not respond to the available conventional pharmacological and non-pharmacological treatment.⁵ In Colombia, after kidney and liver transplantation it is the third most common solid organ transplant performed. From January to November 2015, 1096 transplants were performed in Colombia, 157 of which were heart transplants.⁶ Traditionally, severe psychiatric illness, such as bipolar affective disorder, has been considered a contraindication for the transplant of solid organs.⁷ However, bipolar disorder has been linked with metabolic syndrome and multiple studies have found the prevalence of metabolic syndrome to be higher in people with bipolar disorder than

in the general population (17% compared to 8% in Italy; 27% compared to 19% in Belgium; and 32% compared to 36–49% in the United States). Moreover, people with bipolar disorder are known to have a high cardiovascular mortality rate, possibly as a consequence of the associated risk factors, which include hypertension, obesity, dyslipidaemia and diabetes mellitus.⁸

Although the number of patients on the waiting list increases year after year, the number of patients transplanted remains stable at four to five thousand a year. This is because the number of donors does not increase proportionally, and means that candidate patients have to be carefully selected to ensure they meet the necessary requirements.⁹

The aim of this article is to report the case of a woman with bipolar disorder who required a heart transplant because of ventricular tachycardia refractory to conventional treatment. We describe the assessment and accompaniment process by psychiatry pre-transplant and in the immediate postoperative period.

Methods

Case report and narrative literature review. Informed consent was obtained from the patient after she had been given a clear explanation about the academic use of her clinical information and the confidentiality of the data was guaranteed.

The guidelines established in the Belmont report¹⁰ and the declaration of Helsinki¹¹ were followed. The information search was carried out in MEDLINE and Google Scholar. We selected meta-analyses, systematic reviews and case reports. Articles in English and Spanish, with no time limits, were included. The search criteria were: [ventricular, tachycardia], [heart transplantation] and [bipolar disorder]. In Spanish, the terms used were [trasplante cardíaco], [trastorno bipolar].

Case report

A 34-year-old woman with a history of bipolar affective disorder. The onset of her mental illness was at the age of 13, with altered behaviour that required admission to a psychiatric hospital. She was diagnosed with bipolar disorder type I in view of the characteristics of her symptoms, with delusions of grandeur, hyperthymia, pressure of speech, motor restlessness and general insomnia. She was treated with valproic acid and olanzapine, with full recovery. The patient subsequently discontinued the medications on her own accord and remained asymptomatic until the age of 18, when she had a second manic episode; she then had a third at the age of 31. Both episodes required hospitalisation and pharmacological treatment with mood stabilisers and atypical antipsychotics. She never had suicidal behaviour. Before suffering cardiovascular symptoms, the patient was taking lithium 900 mg/day and aripiprazole 15 mg/day on an irregular basis.

The patient studied up to the first year of *Bachillerato* [A level equivalent] with good academic performance, as she continues to have. At the time she was admitted to hospital, she was working in her own fast-food business. She was living with her foster mother and a 9-year-old daughter, and had recently separated from her partner with whom she had lived for 15 years and had two children. She had no history of head injury or substance misuse/abuse or mental illness in the family.

The patient's mother took her to the accident and emergency department of a general hospital after she "fainted". She was unconscious and in cardiorespiratory arrest on arrival. The attending physicians initiated cardiopulmonary resuscitation manoeuvres. After defibrillation she went into ventricular tachycardia. After arresting for a second time, she was defibrillated once again, but the rhythm of polymorphic ventricular tachycardia persisted.

The patient was transferred to intensive care with invasive monitoring, vasoactive support with noradrenaline and invasive ventilatory support. Electrocardiogram showed prolonged QTc and echocardiogram showed ejection fraction of 25% and dilated chambers. Coronary angiogram detected no lesions. The patient was extubated on day two after admission and regained consciousness with no signs of secondary neurological problems. She had an electrophysiology assessment, from which she was considered to be a candidate for an implantable cardioverter-defibrillator.

She was then assessed by psychiatry, who decided to start pharmacological treatment with aripiprazole 15 mg/day and lithium 600 mg/day, as these were the drugs she had been taking previously. As the ventricular tachycardia was not responding to pharmacological treatments, she was referred to a cardiovascular institution which treats more complex patients to undergo electrophysiological studies, mapping and ablation, and to be assessed for possible implantation of a cardioverter-defibrillator.

While the patient was in intensive care, liaison psychiatry assessed her for the first time by means of an unstructured psychiatric interview, using DSM-5¹² diagnostic criteria. She was found to be calm and collaborated with the interview, recounting the experience she had been through, "I died and they resuscitated me for 20 minutes...". She understood how

serious her heart condition was and expressed her fear of dying.

The mental examination found the patient to be alert, opening eyes spontaneously, making eye contact with the interviewer and orientated in place, situation and person. She was interested in the interview, had no abnormal motor behaviour, attention span normal, euthymic, no abnormal thought content, mentally well, speech and language normal, thinking logical, coherent, no abnormal sensory perception, no depressive cognition or suicidal ideation. She had intact memory, unimpaired judgement, appropriate insight into her disease and positive outlook, for which reason she was considered to fulfil the DSM-5¹³ criteria for bipolar disorder in remission phase.

At the proposal of cardiology, it was decided to discontinue the lithium and aripiprazole as the patient continued to have prolonged QTc. She was started on valproic acid in view of its better cardiovascular profile, initially 750 mg/day, gradually increasing to 1500 mg/day and clonazepam 1 mg/day; with adequate tolerance, valproic acid in blood 84 mg/dl, good sleep pattern and euthymia. After the change in drug therapy, the patient's QTc interval returned to normal.

The electrophysiological studies, mapping and ablation were performed without complications, but the patient continued to have polymorphic ventricular tachycardia. Ablation of the left stellate ganglion was subsequently performed, but without success. The patient's case was discussed with the transplant team, and it was decided that the only medical option was a heart transplant with urgent priority status 0 (absolute priority across the national territory), so liaison psychiatry referral was requested to assess the case.

Liaison psychiatry verified the patient's diagnosis of bipolar disorder, and withdrew the lithium and aripiprazole that were contributing to the prolongation of QTc (that was confirmed when it returned to normal); she was started on valproic acid and clonazepam, two safe psychiatric drugs from a cardiovascular point of view, which have proved effective in preventing decompensation of the patient's bipolar disorder in the pre-transplant and post-transplant stages.

The patient's wish to have the transplant was assessed. She initially expressed anxiety ("Receiving the heart of a stranger", with beliefs, behaviours and desires different from hers). A cognitive-type therapeutic approach was proposed for these irrational ideas aimed at the patient identifying why the idea was irrational and thereby decreasing the negative emotional burden that generated the idea and transforming her initial negativity towards the transplant to seeing it as a positive step, "it's a gift of life that someone is going to give me".

The patient's potential capacity to cope with the challenges of the transplant was assessed; her psychiatric history and the psychopathological findings at the time of assessment were duly reported to the transplant group; close follow-up was provided throughout the entire process (before and after the transplant) to the patient, her family and the treating team, and the patient was put in contact with the general practitioners and psychiatrists of her respective healthcare provision organisation.

Liaison psychiatry assessed the patient and her family again in order to establish why the patient had not adhered to the lithium treatment. They found she had received little

instruction on the importance of adherence to treatment and was of the belief that, if she had no symptoms, she did not need to take the medication. However, with the information that she had received in the previous month from psychology and psychiatry about bipolar disorder, both the patient and her family were obviously motivated to adhere to the drug treatment and the periodic follow-ups by psychiatry. The patient had a strong support network of family and friends.

In addition to liaison psychiatry and psychology, the pre-transplant assessment protocol for the patient included assessment by social work and other medical specialties such as cardiology, electrophysiology and cardiovascular surgery.

After a month in hospital with accompaniment by psychology and psychiatry, both these specialist areas gave favourable opinions for the heart transplant. The patient received her new heart 1.5 months after being placed on the national transplant list.

At the time of writing this case report, nine months had elapsed. The patient was euthymic and had not suffered any relapses. She was still working in the fast-food business. She was fulfilling her role as a mother, taking care of her two children and remained separated from their father. She punctually attended her follow-up appointments with cardiology. She has had to be admitted twice with a diagnosis of acute rejection, each time successfully treated with immunosuppressants and systemic steroids. While in hospital, she had close follow-up through liaison psychiatry, and had no symptoms to suggest decompensation of her bipolar disorder. She was receiving treatment with valproic acid 1500 mg/day and quetiapine 200 mg/night. The last determination of valproic acid was 75 mg/dl. Liaison psychiatry at the clinic where the patient had the transplant has been in communication with psychiatry at the health centre that looks after the patient, to maintain the consistency of the treatment. Support is also provided by psychology and family therapy.

Discussion

This complex clinical case posed the treating physicians a number of different challenges. From a cardiology point of view, a heart transplant was the only option that this patient had if she was to survive, as she was refractory to all the therapeutic options aimed at stabilising the ventricular tachycardia that had caused her cardiorespiratory arrest and exposed her to a high risk of sudden death. From a psychiatric perspective, subjecting a patient with bipolar disorder to severe physical and mental stress could unbalance her affectively.

Psychiatric assessment protocols

The pre-transplant psychiatric assessment protocol of the institution where the transplant was performed for our patient has the following absolute contraindications: a) active substance abuse; b) psychosis that limits informed consent or compliance with medical instructions; c) refusal to have transplant; d) suicidal ideation; e) factitious disorder with physical symptoms, and f) little willingness to participate in the psychoeducational and psychiatric process. Among the relative contraindications are: a) dementia or other persistent brain

dysfunction; and b) psychiatric illnesses refractory to treatment, such as mood disorder with suicidal risk, schizophrenia, eating disorders and personality disorders.

Another protocol for psychosocial assessment pre-transplantation is the SIPAT (Stanford Integrated Psychosocial Assessment for Transplantation),¹⁴ which assesses the patient's knowledge and understanding of their illness, the transplant process, adherence to immunosuppressive treatments, lifestyle, exercise, substance misuse/abuse, social support, psychological stability and underlying psychopathology. It rates each of these aspects. The score classifies the patients as: excellent candidate; good candidate; minimally acceptable candidate; poor candidate; and high-risk candidate.

In our case, the referral to liaison psychiatry was made precisely with the aim of confirming whether the bipolar disorder contraindicated the transplant. However, the goal from the start was to work towards the possibility of transplant, provided the patient's illness was stable and that she wanted the transplant, had the support of her family and, psychologically, had the strategies to take on the challenges that transplantation would impose on her both short and long term.

Psychotherapeutic accompaniment

Liaison psychiatry closely accompanied the patient and family throughout the process, during her time in hospital and the immediate post-transplant period (3 months). Aspects covered in the psychotherapeutic support included the following:

- Adaptation to hospitalisation in the coronary care unit.
- Separation from normal day-to-day roles (mother, wife, businesswoman).
- Fatigue due to prolonged hospitalisation (2 months).
- Visits from family members becoming less frequent.
- Conflicts with the nursing staff (management of schedules, daily routines, diet).
- Fear of dying suddenly (new episodes of circulatory collapse requiring cardioversion).
- Surprise and disbelief post-transplant.
- Anxiety and pain from myocardial catheterisation and biopsies post-transplant.
- Perception of her body having changed and having a "new heart, but empty" of feelings and emotions.

Literature review

There is little scientific literature on heart transplantation in patients with severe mental illness. Coffman et al.¹⁵ reported 35 cases with identified mental illness in a period of two years in 12 transplant centres in the United States, Canada and Australia: schizophrenia (13), bipolar disorder (13), unspecified psychotic disorder (4), major depression (3) and schizoaffective disorder (2). Of these, 37.1% suffered manic or psychotic episodes after the transplant; 20.0% attempted suicide; 5.7% committed suicide; 20.0% suffered from severe depression or catatonia; and 5.7% were arrested by the police for antisocial behaviour. In that series of cases, 14.7% suffered rejection of the transplant due to lack of adherence to treatment; 20.0% had paranoid ideas that interfered with their taking the

medication; and 2.9% suffered from delusions that affected their acceptance of the transplanted organ.

In a three-year follow-up of 191 cardiac transplant recipients to determine the prevalence and risk of depression and anxiety disorders, Dew et al.¹⁶ found that post-transplant 25.5% had major depression, 17% post-traumatic stress disorder, and 38.3% any mental disorder. Among the factors that increased the cumulative risk of a post-transplant psychiatric disorder were the pre-transplant psychiatric history, being female, prolonged hospitalisation, greater functional impairment and scant family support.

Zimbrea et al.¹⁷ reported on 34 patients with a history of psychotic disorder who were candidates for solid organ transplantation. Of these patients, 56% were considered medically and psychiatrically suitable to be on the transplant list; three were rejected or deferred because of psychiatric comorbidity; one was re-assessed and transplanted and the other two died before re-assessment. One patient who had initially been accepted on the waiting list was removed from the list three years later because of psychiatric symptoms and lack of adherence to treatment. In addition, four patients with no history of psychosis suffered a psychotic disorder after transplantation.

Price et al.¹⁸ conducted a review in 2014 that explored the existing scientific evidence on the prognosis of patients with psychotic disorders undergoing solid organ transplantation. They concluded that the information available to determine whether psychotic disorders prior to transplantation increase the risk of poor adherence and worse post-transplant prognosis was scarce and insufficient. The little evidence available confirms that social isolation is a key factor for poor adherence post-transplant. From this scant evidence, the authors conclude that psychotic disorders alone should not be considered sufficient reason to exclude a patient with psychotic disorder from a transplant protocol.

In a recently published article, Rosenberger et al.¹⁹ found that, in a group of 178 lung transplant patients, those with early post-transplant major depression had an increased risk of bronchiolitis obliterans (hazard ratio [HR]=1.65; 95% confidence interval [95% CI], 1.01-2.71) and graft rejection (HR=1.75, 95% CI, 1.062-2.88). In 2008, Hategan et al. published the case of a 65-year-old man who received a heart transplant; two years later he was seen by psychiatry because he wanted to stop the immunosuppressant medication, and he was diagnosed with bipolar disorder.²⁰ The authors stress the importance of social support and follow-up of these patients during all stages of the transplant process. Another recent case report is that of a 46-year-old male with a heart transplant. In the pre-transplant period he had anxiety and depressive symptoms, for which cardiology referred him. He was started on antidepressant treatment, with partial improvement of symptoms. Two months after the transplant, he separated from his wife, the anxiety and depressive symptoms worsened and he had an acute rejection of the graft. An emergency plan was set up to provide psychosocial support and support for adherence to treatment. However, one year after the transplant, the patient died of a cardiac arrest. It was later discovered that the patient had stopped taking his immunosuppressants one week before his death and had gone back to drinking alcohol and smoking cigarettes. The authors point out the importance of psychosocial support and the negative

consequences of affective symptoms for the general prognosis of a transplant patient.²¹

Lastly, this case report shows that it is possible to offer a heart transplant to a patient with bipolar disorder when psychiatry and psychology participate in the transplant groups, providing accompaniment to these patients throughout the process.

We also reaffirm the importance and the necessity of continuing to conduct research in this interesting area, so that better scientific evidence may guide the decisions made by transplant teams concerning psychiatric patients.

Ethical disclosures

Protection of human and animal subjects. The authors declare that the procedures followed were in accordance with the regulations of the relevant clinical research ethics committee and with those of the Code of Ethics of the World Medical Association (Declaration of Helsinki).

Confidentiality of data. The authors declare that they have followed the protocols of their work centre on the publication of patient data.

Right to privacy and informed consent. The authors have obtained the written informed consent of the patients or subjects mentioned in the article. The corresponding author is in possession of this document.

Conflicts of interest

The authors have no conflicts of interest to declare.

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