

## QUETIAPINE IN MANAGEMENT OF MANIC SYMPTOMS IN PATIENT WITH HEART TRANSPLANTATION – A CASE REPORT

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### INTRODUCTION

Heart transplant is a common transplant procedure which is a therapeutic option for people with end stage heart disease. The available literature showed mixed results in continued pharmacological therapy for previous mental illness in individuals who underwent a transplant procedure. However, there is no available randomized trial and no consensus exists within the medical community about absolute or relative contra-indication for organ transplant, with the exception of active substance abuse. Unfortunately many transplant programs worldwide find mental disorders relative or absolute contraindication for transplant (Mehra et al. 2006).

We report a case of mania in a 65-year-old Caucasian male with past medical history pertaining to psychiatric problems, hypertension, chronic renal insufficiency, non insulin dependent diabetes mellitus and heart transplantation.

### CASE REPORT

Our patient is a 65 year old man with longstanding history of psychiatric problems. In February 2006 he was brought to psychiatric emergency room because of agitation, aggressiveness, hyperactivity and inappropriate behavior. He was previously hospitalized in 1978 for manic symptoms with psychotic characteristics. Following that episode he was treated as an outpatient until 1982. Since then, he was completely functional and worked as a factory worker. He occasionally complained about flashes of depressive mood; however, he was able to handle them without any medication. His past medical history includes hypertension, chronic kidney disease, diabetes mellitus type 2 and cardiomyopathy. His cardiac problems started in the mid 1990s with dilatative cardiomyopathy, atrial fibrillation followed by heart failure which resulted in heart transplantation in March 2004. Preoperatively, he was seen by a psychiatrist who gave clearance for the procedure since his mental health was in full remission.

Currently, he is retired, married, has four children and lives with his family. He denied smoking, alcohol or drug abuse. His psychiatric family history was negative. On admission in 2006, his medication included: cyclosporine, mycophenolate mofetil, prednisone, acyclovir, amlodipine, bisoprolol, indapamide, ranitidine, glicazide, metformine and fluvastatine.

His head, neck, lung, abdominal and neurological exams were without pathological findings. A heart exam was within normal limits. Hematological parameters and basic biochemistry were normal. A urine drug screen was negative.

The patient had very poor hygiene. Few pills of sildenafil citrate were found in his pocket. He was oriented; cooperative, quite talkative, albeit with pressured speech. He denied that anything was wrong with him and was quite hostile toward his family. He expressed persecutory ideas about his sons since they were against his ideas of selling property. He became psychomotor agitated whilst on the issue. His sons complained about his decreased need for sleep as well as his hyperactivity. He did not have any delusions; however, he had grandiose ideas and plans.

The patient was admitted to an inpatient psychiatric unit with a diagnosis of mania without psychotic elements and was introduced on a therapy with quetiapine (100/0/100 mg at day 1, 100/100/100 mg at day 2 and 100/200/100 mg at day 3). His condition improved significantly, measured with Clinical Global Impression/Improvement Scale (Guy, 1976) and he was discharged home on the 11th day with the diagnosis of bipolar disorder on 400 mg of quetiapine daily. His condition is still well controlled with the prescribed regimen; he is fully functional. He regularly follows up with his psychiatrist as well as an internist and he had one more successful major surgical procedure, artificial knee implant.

### DISCUSSION

Heart transplantation is a complex procedure that carries risks and is very challenging from a surgical, immunological and psychological point of view even in

patients without manifest or recognized mental disorders. Moreover, in the case of our patient and the population he represents, these would also include pharmacokinetic and issues of legitimacy.

According to Listing Criteria for Heart Transplantation only mental retardation and dementia may be regarded as a relative contraindication to transplantation (Mehra et al. 2006). Other specific psychiatric disorders' are not listed. Nevertheless, psychosocial evaluation section includes poor compliance with drug regimens as a risk factor for graft rejection and mortality (Mehra et al. 2006). Indeed, the number of rejection episodes was associated with global psychosocial risk (Shapiro et al. 1995). The general agreement exists that heart transplantation should be reserved for those patients most likely to benefit both in terms of quality of life and survival (Mehra et al. 2006). This present ethical dilemma and might put patients with psychiatric disorders in unequal position, with cardiac programs as the most stringent, both in criteria and in rate of refusals (Levenson & Olbrisch 1993). There was considerable disagreement among programs when a patient is rejected on psychosocial grounds. More than 70% of all programs excluded patients for transplantation on the grounds of dementia, active schizophrenia, current suicidal ideation, history of multiple suicide attempts, severe mental retardation, current heavy alcohol use, and current use of addictive drugs. The proportion of patients rejected for transplantation on psychosocial grounds ranged from 0% to 37%, with an average rate of 5.6% in the United States and 2.5% in non-U.S. programs (Olbrisch & Levenson 1991). Therefore, psychiatric involvement in transplant medicine is essential.

As it was illustrated in this case, our patient was referred to a psychiatry service with the appearance of manic symptoms almost two years after the heart transplant. According to available data and diagnostic assessment, his condition satisfied DSM-IV-TR criteria for manic episode of bipolar disorder (APA 2000). We propose that some of his medication may have caused exacerbation of the underlying psychiatric disease since it was already described in the literature: mania caused by interruption of steroid therapy (Venkatarangam et al. 1988), case of resistant bipolar disorder caused by steroid therapy (Pies 1981) and reactivation of stable bipolar disease after steroid usage (Goldstein & Preskorn 1989).

Cyclosporine was also the suspected cause of psychiatric alteration (Craven 1991) as well as acyclovir which could induce mania (Fukunishi et al. 1994). There is a possibility that his condition is caused solely by prescribed medication; however, that cannot explain his previous psychotic episode as well as self reported occasional depressive mood.

Second generation or atypical antipsychotics are increasingly used in the management of acute mania. The effectiveness of the atypical antipsychotics in manic states has been shown and there is suggestion that

when an antipsychotic agent is needed, preference should be given to an atypical antipsychotic over the classic drug (Jarema 2007).

We decided to treat our patient with quetiapine which is indicated for the treatment of acute manic episodes associated with bipolar disorder as monotherapy or in combination with mood stabilizers (Vieta 2005). Quetiapine showed long term mood stabilizing features as monotherapy or as part of regimen (up to 12 months) and successfully prevents relapses and has a good safety and tolerability profile (Altamura et al. 2003). Generally, antipsychotics are associated with a range of adverse effects, one of them being tachycardia due to the drug's anticholinergic properties. However, in the case of our patient who has also had a heart transplant, quetiapine, an atypical antipsychotic, has proven to be safe and effective in treating mania.

Since our patient also has diabetes mellitus, it was appropriate to treat him with an antipsychotic agent with less effect on blood glucose levels such as quetiapine or aripiprazole which was not approved at that time in Croatia (Guo et al. 2006). Also, elevated prolactin levels might be involved in solid graft rejection. Regarding this, typical antipsychotics with low influence on prolactin levels as aripiprazole or quetiapine should be preferred (Foley & Kast 2006).

This case demonstrates the safety and efficacy of quetiapine as monotherapy in an acute intervention, as well as long-term maintenance treatment in a heart transplant patient with bipolar affective disorder and multiple medical problems. Despite the fact that quetiapine was not associated with any clinically significant adverse effect after 12 months of treatment in our patient, we do believe that pharmacotherapy of manic symptoms should be used with caution in heart transplant patients, with decisions made on a case-by-case basis, until a larger database on safety is available.

## CONCLUSION

This case also shows that a patient diagnosed with mental illness could adhere to rigorous pre and post-transplantation procedures and that mental illness should not be an absolute contraindication for transplantation. Generally, organ transplantation is considered to be very emotionally distressing for patients and psychiatric involvement in transplant medicine is essential. This is especially true for patients with mental illnesses. In this case report, we want to emphasize that certain psychiatric conditions should not be a contraindication for transplant as they can be very well managed; however, previous mental evaluation is necessary.

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**Conflict of interest :** None to declare.

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