

Lessons Learned from the Amputation of a Bilateral Hand Grafted Patient due to Psychiatric Disorders

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Summary: The importance of psychosocial aspects in upper extremity transplantation (UET) has been emphasized since the beginning of the vascularized composite allotransplantation era. Herein a long-term UET failure mainly due to psychiatric disorders is reported. A young woman amputated in 2004 (electrocution) underwent bilateral UET in 2007. At the time of transplantation the patient underwent a psychological evaluation, which did not completely consider some traits of her personality. Indeed, she had an anxious personality and a tendency to idealize. The trauma of amputation, the injuries associated with the accident, and the short delay between the accident and the transplantation elicited vindictiveness, entitlement, and impulsivity. Following transplantation, she had a high anxiety level, panic attacks, depression, and hypomanic episodes. She was poorly compliant to the rehabilitation program and the immunosuppressive treatment. She developed 13 acute rejection episodes (reversed by appropriate treatment) but neither clinical signs of chronic rejection nor donor specific antibodies. She developed many severe complications due to the treatment and the psychiatric disorders. At her request, after many interviews, the allografts were removed in 2018. Pathological examination and an angiography performed post-amputation revealed signs of graft vasculopathy of varying severity, in the absence of clinically overt chronic rejection. This case highlights the need to detect during the initial patients' assessment even mild traits of personality disorders, which could herald psychiatric complications after the transplantation, compromising UET outcomes. It further confirms that skin and vessels are the main targets of the alloimmune response in the UET setting. (*Plast Reconstr Surg Glob Open* 2020;8:e2905; doi: 10.1097/GOX.0000000000002905; Published online 27 October 2020.)

The patient's ability to successfully navigate the complexities of post-transplant life is of paramount importance for the long-term outcomes in upper extremity transplantation (UET). The importance of psychosocial aspects in this new type of transplantation has always been emphasized but not fairly evaluated at the

beginning of the vascularized composite allotransplantation era.¹ Consequently, the approach of the various teams varies, and so far no consensus on the optimal psychosocial evaluation and management of the patients exists.^{2,3} Herein we report a long-term failure in UET mainly due to psychiatric disorders and the lessons learned from this case.

CASE REPORT

The recipient, a 27-year-old woman, lost both hands after electrocution on August 28, 2004, with amputation at the mid forearm level on both sides.⁴ Before the accident she was single and an athlete. She had an anxious personality and a tendency to idealize, which was not considered an absolute contraindication to the UET. However, the trauma of amputation, the accident-induced injuries, and the relatively short delay between the accident and the transplantation elicited vindictiveness, entitlement,

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and impulsivity, which she used as a defense mechanism against depressive tendencies that resurfaced after the accident.

The patient was transplanted on 19.02.2007. The donor was a brain-dead 40-year-old woman. The immunosuppressive induction treatment included tacrolimus, mycophenolate mofetil, prednisone, and antithymocyte globulins (Thymoglobulin, Genzyme) during the first five days. The maintenance therapy included tacrolimus (targeted trough levels 8–10 ng/mL), mycophenolate mofetil (2 g/d), and prednisone (5 mg/d).

In the immediate post-operative period the patient suffered severe neuropathic pain, but she easily accepted the grafted hands, considering them as “own” in the early post-transplant period. She developed 13 biopsy-proven acute rejection (AR) episodes (Table 1), which were completely reversed by the treatment. She never developed clinical signs of chronic rejection nor donor-specific anti-HLA antibodies during the follow-up, even during AR episodes.

The patient was not entirely compliant to the rehabilitation program, and not always to the immunosuppressive treatment, performing self-medication. She continued to be a heavy tobacco smoker. Although the functional recovery was good,^{4,5} she had the lowest scores of quality of life among our bilateral UET recipients, according to the RAND-36 measure of health-related quality of life survey.⁵

To prevent AR episodes, the patient’s immunosuppressive protocol had to be changed on several occasions. The follow-up was studded with several complications (Table 2) caused by the maintenance immunosuppressive therapy, the additional treatment for the numerous AR episodes, and by psychiatric disorders that occurred. The patient developed eating troubles (she became obese

and diabetic 7 years post-transplantation), hypertension, and hypercholesterolemia. Until 2014 the patient’s renal function was good. Serum creatinine and calculated glomerular filtration rate (GFR) using simplified modification of diet in renal disease were normal in the first post-transplant period; afterwards, however, the renal function slowly decreased with GFR around 50 mL/min before amputation.

The patient appeared to be in denial of the constraints and limitations imposed by her transplantation and did not take sufficient care of hands (namely she did not protect them from exposure to cold and to traumatism). In August 2008, 1.5 years post-transplant, she suffered a severe depressive episode that necessitated treatment with antidepressants and anxiolytics; she then suffered a manic episode. During the follow-up, depression and anxiety relapsed but were controlled by the treatment; however, the patient continued to make unrealistic requests concerning her treatment. She experienced frequent panic attacks caused by the fear of graft rejection. She had periodic psychiatric follow-up in her residence place, but a regular local psychiatric follow-up was not possible because of multiple conflicts with psychologists and psychiatrists. Her mood lability and other behavioral traits were consistent with a borderline personality disorder and possibly with bipolar diathesis.

The psychological and medical complications of the transplantation prompted the patient to require removal of the grafts. After several interviews, the allografts were removed on September 13, 2018. After the graft removal, the patient appeared relieved, as she had been unable to sustain the constraints of the immunosuppressive treatment and the follow-up.

Table 1. Episodes of AR

Date of AR Episodes	Banff Grade	Treatment
March 2007		
(1 post-Tx month)	II	IV Steroids (3 boluses of 1 g)
November 2007	II	IV Steroids (3 boluses of 1 g)
(9 post-Tx months)		
September 2008	III	ATG (75 mg/d for 6 days)
(1 year and 7 months post-Tx)		
September 2009	II–III	Increase in oral steroid dose
(2 years and 7 months post-Tx)		
November 2010	II–III	Campath-1H (20 mg)
(3 years and 9 months post-Tx)		
March 2011	III	Campath-1H (20 mg)
(4 years and 1 month post-Tx)	Capillary thromboses	
March 2012	III	Campath-1H (20 mg)
(5 years and 1 month post-Tx)	Capillary thromboses	
March 2013	III	Increase in oral steroid dose
(6 years and 1 month post-Tx)		
July 2013	II–III	Autologous adipose mesenchymal cells and steroids (1 mg/kg)
(6 years and 5 months post-Tx)	Capillary thromboses	Autologous adipose mesenchymal cells
October 2014	III	
(7 years and 8 months post-Tx)	Capillary thromboses	
February 2016	III	Increase in oral steroid dose
(9 years post-Tx)		
January 2017	III	Increase in oral steroid dose
(9 years and 11 months post-Tx)	Capillary thromboses	
June 2018	I–II	Steroid and tacrolimus creams
(11 years and 4 months post-Tx)		

Post-Tx, post-transplantation; ATG, Antithymocyte globulins.

DISCUSSION

The salient psychiatric issue of this case is that a pre-existing personality disorder was exacerbated by multiple successive traumatic events. On the basis of knowledge of that time, her mood was not considered a contraindication to the transplantation. Consequently, the first learned lesson is the need to detect during the initial patient's assessment even mild traits of personality disorders, which could herald significant psychiatric complications (namely depressive or/and anxious symptoms) after UET. These symptoms influenced the patient's compliance and ability to cope, her relationship with the members of the team and her unrealistic expectations. The constraints of the treatment and of the rehabilitation program, the occurrence of AR episodes, and complications activated her affective dependency on the team and caused major anxiety.

The second lesson is that psychosocial disorders may influence UET outcomes. The many AR episodes and complications were partly due to non-adherence to the treatment, self-medication, smoking habit, and feeding disorders. Moreover, she did not avoid exposure to cold and traumatism of the grafted hands, factors that may promote AR.⁶

The third lesson is the discovery of vascular lesions in the amputated grafts in the absence of obvious clinical signs of chronic rejection (See **document, Supplemental Digital Content 1**, which displays Microscopic and vascular alterations in the removed allografts. <http://links.lww.com/PRSGO/B499>) (See **figure, Supplemental Digital Content 2**, which displays Histopathology of the amputated grafts (Hematoxylin-eosin-saffron stain). A. An arteriole surrounding the left proximal ulnar artery shows some degree of wall thickening and luminal narrowing, and lymphocytic infiltration. B. Left palmar artery: wall thickening with discontinuous elastic lamina and luminal thrombosis. <http://links.lww.com/PRSGO/B500>) (See **figure, Supplemental Digital Content 3**, which displays Angiography of the right (A) and (B) the left hand after the amputation. The palmar arch and the principal thumb arteries are present on both hands, although the latter was thin on the right hand. Thrombosis of the third palmar

interosseous artery is present on the left side (black arrow) while on the right side it was present but thin. One of the arteries of the 2nd, 3th, 4th, and 5th right finger; one of the arteries of the 2nd, 3th, and 5th left finger; and both arteries of the 4th finger are not filled. <http://links.lww.com/PRSGO/B501>)

In conclusion, the risk/benefit balance in VCA is subtle. The patient reported here was very satisfied with her hand grafts and even before the amputation she considered the UET a “benefit,” but she was unable to cope with the long-term constraints of the treatment, hospitalizations, examinations, AR episodes and complications. Consequently, the selection of UET candidates must be strict, considering all the possible mild personality disorders, which can compromise the outcome of the transplantation.

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