The Advent of Vascularized Composite Allotransplantation

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KEYWORDS

• Allotransplantation • Composite tissue grafting • Tissue transfer

KEY POINTS

- The ultimate utility of VCA is the provision of functional restoration and improvement in quality of life.
- To this end, developments in peripheral nerve regeneration may allow for greater functional return after upper extremity loss at more proximal levels (ie, upper arm, above elbow).
- Additional advances in the treatment of autoimmune dermatologic disease may provide new insights into mechanisms to achieve tolerance of skin in VCA.
- The future of VCA is bright and most likely involves advances in basic science and clinical protocols to achieve the ultimate goal of immunologic tolerance.

Modern microsurgical techniques have made possible a broad spectrum of novel means for the reconstruction of complex bone and soft tissue defects. These techniques, in combination with developments in transplant immunology, have led to successful hand and facial allotransplantation and achievement of the highest rung in the reconstructive ladder – truly replacing like with like.

The utilization of contemporary microsurgical technique in the context of vascularized composite allotransplantation (VCA) (1) permits successful technical execution and feasibility of VCA, (2) facilitates the study of immunologic tolerance in VCA preclinical models, and (3) optimizes functional VCA outcomes.

TECHNICAL FEASIBILITY

To date, the world experience in VCA includes more than 100 upper extremity, 30 craniofacial, and various other types of composite soft tissue transplants, including the abdominal wall, lower extremity, and genitourinary region across different patient age groups. At the Massachusetts General Hospital (MGH), the authors have performed a left upper extremity VCA in a left-hand dominant patient who was 9 years' status–post 50% burns of his total body surface area with prior extensive débridement and skin grafting and a metacarpal amputation of his left hand without excellent function. His burns resulted in the absence of cutaneous veins in the forearm, which presented a challenge for venous outflow of the allograft. This technical challenge was successfully overcome with a volar forearm fasciocutaneous extension technique (**Fig. 1**) incorporating proximal vascular anastomoses and distal neurorrhaphies for the synergistic effect of improved perfusion and minimizing the length of neural regeneration to expedite functional recovery.[1] At

The authors have nothing to disclose.

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Clin Plastic Surg 44 (2017) 425–429

http://dx.doi.org/10.1016/j.cps.2016.12.007

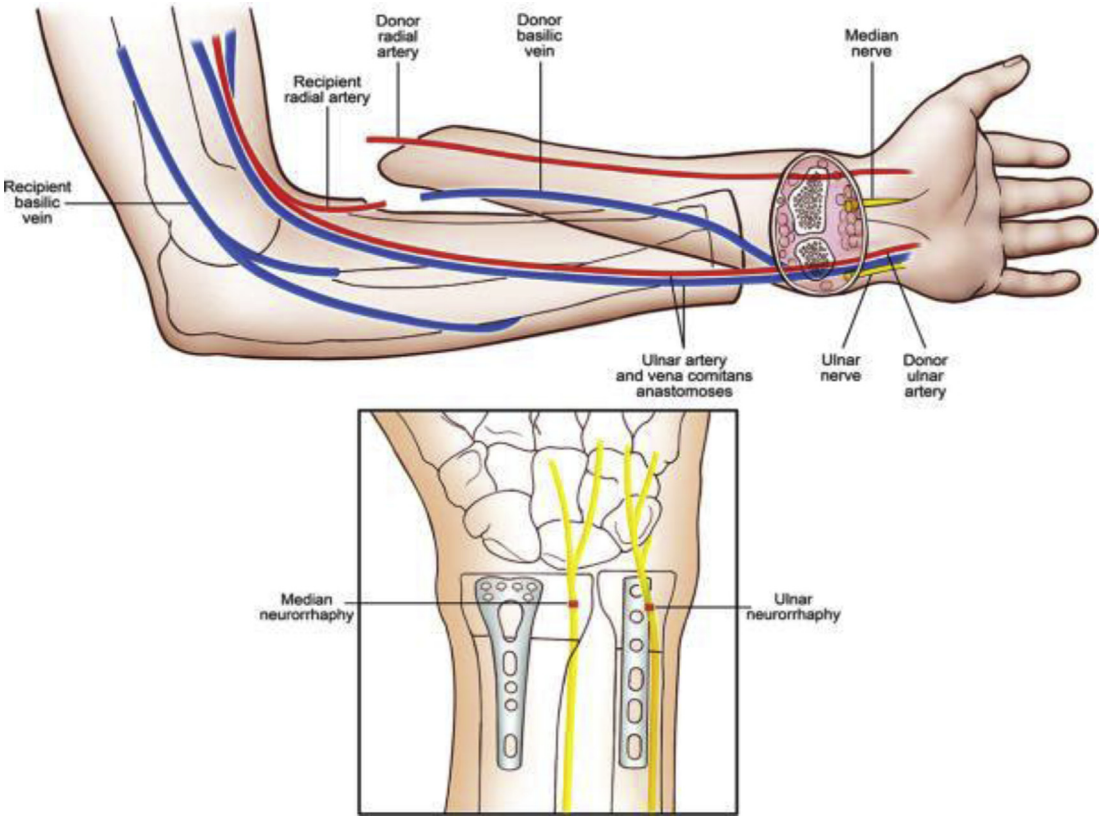

Fig. 1. Operative plan: (1) osteosynthesis at 3 cm proximal to radiocarpal joint; (2) ulnar artery and vena comitans anastomoses in distal forearm proximal to wrist crease; radial artery, vena comitans, and basilic vein anastomoses in proximal forearm immediately distal to antecubital fossa; (3) digital flexors adjusted to achieve natural cascade and single-weave, Brown side-to-side tenorrhaphy for all tendons; and (4) median and ulnar neurorrhaphies at wrist flexion crease. (*Reproduced from* Eberlin KR, Leonard DA, Austen WG Jr, et al. The volar forearm fasciocutaneous extension: a strategy to maximize vascular outflow in post-burn injury hand transplantation. Plast Reconstr Surg 2014;134:733; with permission.)

3 years' post-VCA, the patient has regained good strength and sensibility in the left hand, with an intrinsic power of 4/5 and a Disabilities of Arm, Shoulder and Hand score of 27.

Despite the ever-increasing numbers and types of VCAs, patients who have received such allografts are necessarily maintained on various combinations of lifelong immunosuppressive regimens that are modeled after those used in solid organ transplantation. The potential sequelae of such chronic immunosuppression are well known, and patients who are recipients of VCA have developed myriad complications, including chronic allograft loss, metabolic disorders, renovascular dysfunction, opportunistic infections, and neoplasms.[2]

IMMUNOLOGIC TOLERANCE APPROACHES

Mixed Chimerism

Building on the clinical success of the authors' transplant center colleagues in achieving immunosuppression-free renal transplantation based on the establishment of mixed chimerism,[3] the authors' current laboratory efforts in VCA are directed at the adoption of this approach for the induction of immunologic tolerance. This protocol involves nonmyeloablative conditioning and hematopoietic stem cell transplantation (HSCT) of the VCA recipient so that coexistence of the immune cells of both donor and recipient can be achieved in the absence of destructive immunologic responses (**Fig. 2**).

Importance of Stable Mixed Chimerism

The authors have recently demonstrated, for the first time, that all components of a fasciocutaneous VCA, including the epidermis, can be accepted indefinitely in a unique MGH miniature swine model. Using the authors' previously described protocol, haplomatched animals (SLA^{AC} donors and SLA^{AD} recipients) are