Facial Transplantation

Daniel Alam

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Abstract The evolution of facial reconstruction has seen significant advances over the last century. The advent of microsurgical techniques created the ability to transfer autogenous tissue from donor sites across the body, allowing complex defects to become amenable to reconstruction. Despite all of these advances, the fundamental limitation of free tissue transfer is the inability to repair complex neuromuscular defects, especially those in the mid-face. While the concept of allograft transplantation and its use has been widely accepted in the arena of solid organ transplantation, the concept of skin transplantation is relatively new with the first successful hand transplant that occurred in 1998. Facial transplants followed in 2005 (Devauchelle et al. *Lancet* 368:203–209, 2006). This technique offers a potential solution for these neuromuscular mid-face injuries that cannot be reconstructed with traditional approaches. This article discusses the limits of conventional reconstruction, the rationale for facial transplantation, and the clinical outcomes of two cases of near total facial transplants. Both patients have had excellent short- and long-term outcomes. The future of this technique and its role in facial reconstruction appears promising.

Keywords Facial transplantation · Allograft · Microvascular reconstruction · Facial reconstruction · Transplant · Facial trauma · Mid-face injury

Introduction

The field of facial reconstruction has made remarkable strides over the last century. Injuries and defects that were once considered impossible to reconstruct have become amenable to modern techniques that are now considered standard of care. The evolution has seen us advance from the early developments of local soft tissue flaps and rigid fixation in reconstruction to the advent of microsurgical free tissue transfer. Complex three-dimensional facial defects can now be repaired using these free flaps. This has allowed us to not only simply coapt the residual tissue but also effectively replace significant amounts of tissue that is missing. From the early reports of free flaps in the 1980s to the complex reconstructions of present day, flaps themselves have undergone their own evolution. Time has made the extraordinary into ordinary. Flaps can be molded, pre-laminated, and modified extensively to allow better reconstructions in our patient population. Despite all of these advances, there are certain defects and injuries that we encounter in clinical practice that still remain difficult challenges.

Limitations of Conventional Reconstruction

The ultimate difficulty of facial reconstruction lies in the intrinsic complexity of the face both in form and function. The face is composed of unique three-dimensional structures consisting of a wide variety of tissue types. The variation present makes identification and transfer of appropriate donor tissue to this area sometimes challenging. The unique skin color, texture, and consistency of facial skin are often best reconstructed from adjacent areas within the face. Skin from distal extremities, while

D. Alam (✉)
Queen's Medical Center, Honolulu, HI, USA
e-mail: dan.alam@hotmail.com

effectively transferred through microvascular techniques, is often not appropriately color matched to the face and becomes easily noticeable in the patient. The face also has unique structures that bear no similar homologs in other parts of the body, such as eyelashes and eyelids. The complex spatial relationships and varied tissue types of facial components, such as the nasal base to the upper lip and the junction of the red and white lip at the vermilion, create reconstructive challenges that are not easily overcome. Microvascular reconstruction of the face with the best outcomes is usually seen in cases of complex subcutaneous and bony reconstruction where the skin and SMAS envelope of the face are unaffected by the injury or surgical resection. When the neuromotor components of the face or facial skin is missing, the reconstruction of these areas becomes much more difficult using conventional techniques, as harvest sites do not exist. Flap modification and revision can allow a progressive molding of the tissue to better approximate the desired endpoints but there are obviously limitations to this approach.

The difficulties in achieving the form of the face given its complexity, while daunting, are actually not the most significant limitation to conventional reconstruction. Repair of function is actually a much bigger obstacle. Free flaps (with very few exceptions) are static structural tissue transfers. Any motor function is due to residual muscle function in the face. An example would be a mandibular reconstruction with a fibula flap that relies on native function of the muscle of mastication to work. Our face moves under complex discrete neuromuscular orders directing all of its activity—we smile, laugh, eat, speak, and blink. The ability to communicate emotions with our facial functions has no substitute. Any successful reconstruction of the face from a functional standpoint can not simply be limited to a replication of form but also needs to make this essential connection to the brain. It is this movement of the central face that is the critical component of all of its functional roles. Almost every facet of human communication and socialization relies on this. At a more esoteric level, yet probably as important in essence, the central face is our window to our human emotion. We express anger, joy, grief, and love through the subtle and delicate movements of this part of our face. Injuries to this area not only affect the individual who suffers them but also affects all of those around them. Unfortunately, as surgeons, while we have become adept at moving bone, skin and soft tissue from one region of the body to another, we are still quite limited in our ability to establish a functional neuromuscular reconstruction. The only widely used clinical application of a neuromuscular flap in the face is the gracilis muscle for smile reconstruction. Although the results are excellent for this indication, the limitations of this procedure are obvious. The gracilis muscle is used

primarily to reconstruct only the muscular component of the face and requires the remaining soft tissues and other structures to be intact and uninjured to achieve optimal results. The procedure is in principle solely the replacement of the critical zygomaticus major and minor complex. But, other significant reconstructive challenges remain. How do we reconstruct facial defects when the other facial muscles (orbicularis oculi and oris) are missing? What are the options when facial skin and soft tissue are also missing?

These challenging questions arise when the face is injured by ballistic trauma. The restoration of bony landmarks and closure of soft tissue wounds are often not possible due to the loss of viable soft tissue and bone. Additionally, the inherently poor vascularity of the severely traumatized tissues that remain and the associated evolving tissue necrosis and infection makes a challenging situation worse. Primary repair of the injured tissues is rarely feasible because adequate viable tissue is no longer present locally. The paradigm must shift from the classical conceptions of injury repair to rebuilding. Successful restoration of form and function can only be achieved by recruiting tissues to rebuild the deficient structures of the face.

The treatment approach for extensive traumatic head and neck injuries has shifted away from delayed repair to early repair with local tissue and free tissue transfer reconstructions. Staged early definitive reconstruction allows for fewer surgeries and shorter hospitalizations. The initial repair may involve some elements of healing with secondary intention or primary closure but usually requires early recruitment of healthy tissue into the face via local tissue rearrangement, pedicled regional flap, or free tissue transfer (anterolateral thigh flap and osteocutaneous fibula flap). Local tissue advancement with a cervicofacial flap can be used to reduce the soft tissue deficit and provide skin coverage. Although this flap brings healthier adjacent tissue into the defect, it is a randomly based flap and susceptible to vascular compromise and distal flap necrosis. Pedicled regional flaps (paramedian forehead flap, deltopectoral flap, and latissimus dorsi flap) are supplied by a vascular pedicle allowing for greater tissue viability and versatility. The paramedian forehead flap can be used for nasal reconstruction. The deltopectoral flap and latissimus dorsi flap can be used to reconstruct large skin defects of the neck, lateral face, and scalp.

The evolving success and reliability of microvascular surgery have led to the early use of healthy vascularized free tissue transfer for trauma reconstruction. The advantages of recruiting non-traumatized naive tissue for the reconstruction include a more physiologic restoration of function and a reduction in scar contracture. Free tissue transfer also allows for the reconstruction of varying tissue

Fig. 1 The central neuromuscular face is shown in the *colored* segment of the illustration. The static fasciocutaneous face is shown in black and white (Color figure online)

defects (mucosa, bone, skin, and soft tissue) with comparable vascularized tissue. The anterolateral thigh flap can be used to reconstruct large skin and soft tissue defects. The osteocutaneous fibula flap can be used to reconstruct orbito-maxillary and mandibular defects. Many of these cases are illustrated in another chapter of this issue on free tissue transfer.

While the results are excellent, a few take-home points are warranted. All of the cases shown do not have significant neuromuscular losses of the central face. As discussed above, conventional microsurgical reconstruction alone cannot effectively provide a neuromuscular reconstruction of

significant facial defects. One can think of the face as having two distinct physiological regions. The majority of the face and neck is composed of fasciocutaneous structures that are easily amenable to microsurgical and conventional reconstruction. The central face, however, has significant neuromuscular functions and uniquely complex structures that are quite distinct. This relationship is schematically shown in Fig. 1. Here our traditional techniques are grossly inadequate.

The Importance of the Central Face

The consequence of our limitations in facial reconstruction of the central face is magnified by the incredible importance this area has for our quality of life. The functional significance of the area is obvious. Much of our communication is dependent on the function of our lips and mouth. Labial sounds such as “B” and “P” are common in almost all languages, and they cannot be articulated without lip function. The function of the orbicularis oris is critical for eating and drinking. Nasal function and form is important to establish a safe and appropriate airway. Eyelid function is critical for maintaining our ability to see. These represent just a few of the myriad of vital functions our faces play in terms of our daily existence.

This is not to say that this is the only reason why mid-facial injuries are so devastating. The central face is also the key to our physical identity. We are recognized by the interplay of the structural relationship between our eyes, nose, and lips more so than any other part of our body. Within this small region that is less than 5 % of our body surface area is the foundation of our personal identity. This concept is illustrated in Fig. 2.

The incredible precision of human facial recognition is remarkable. We are able to distinguish over 200,000 independent faces from each other. Within 50 h of birth,

Fig. 2 On the *left* is the entire face. On the *right* is just the central neuromuscular component but preserves the individual’s identity

Fig. 3 The angioneurosome concept with flap design based upon preservation of vascular supply and transfer of a functional neuromuscular unit. On the *left*, the facial innervation is demonstrated. On the *right*, the individual functional regions are illustrated

newborn infants are able to recognize their own mothers from other individuals. The secondary consequences of this are profound. A mother shown images of her children activates rewards and socialization centers of the brain associated with feelings of positive emotions. These responses are unique and distinct to those seen when a mother is shown images of other children versus when she is shown them of strangers. The face offers the key to our human connection. The bonds we developed between our friends and our families are based on recognition of this critical region. There is data to suggest that neuro-chemical relationships of human emotions are based initially on facial recognition that is the foundation for subsequent synaptic relationships to other centers of the brain.

Patients with significant mid-facial injuries with severe disfigurement often claim that they feel disconnected from society. The neuro-physiologic data would suggest that this is a problem that actually lies within the observer—not the injured patient. If someone does not have a face, it is almost impossible for us as observers to develop a normal human relationship with him or her. The majority of patients who seek complex facial reconstruction with these types of injuries are not seeking a surgical procedure to return them to their pre-injury state. They simply would like to have the ability to return to human society [1•, 2, 3].

The Rationale for Facial Transplantation

The complex movement of the mid-face and its critical importance to our lives means effective central facial reconstruction has to be a neuromuscular reconstruction. Simply replacing like tissue with like without re-establishing the connections to the brain results in a sub-optimal mask-like outcome. This result can be more disturbing than the defect itself in certain cases. The movement of this area must be natural with function that allows the patient to rejoin society. Since this cannot be re-created by borrowing tissue from another part of one's own body, the following question arises. What if we were to replace the same neuromuscular tissue complex from another individual?

The resultant solution to this complex reconstructive challenge has been the use of allograft flaps. Facial transplantation has been used to reconstruct severe facial trauma injuries when massive loss of facial structures occurs. While technically more challenging than the typical free tissue transfer and requiring lifelong immunosuppression for the recipient, face transplantation allows a composite transfer of varying skin, soft tissue, and bone that replaces the lost tissue with an exact anatomic and functional match.

Traditionally, flaps have been viewed as the tissue that is recruitable within the angiosome of its pedicle vessel. To understand the rationale for facial transplantation, this concept needs to be extended to the idea of an “angioneurosome.” This concept is illustrated in Fig. 3. The design of the flap is based not only on the preservation of its blood supply but also on the concept of transferring a neuromuscular unit along with its muscular origin and insertion, including rigid facial structures and cutaneous ligaments. If this angioneurosome can be transferred in its entirety, it can be used to replace deficient tissue in a functional manner. Vascularization provides for tissue viability, and then selective coaptation to the corresponding peripheral nerve restores movement and sensation. In doing so, we have the option of not simply reconstructing a mask-like facial form, but rebuilding the face from a functional perspective. Isolating each of the divisions of the facial nerve within an allograft specimen, for example, allows the surgeon to sequentially and segmentally rehabilitate the face [4•, 5].

Medical Risks

Facial transplantation procedures require a lifelong regimen of immunosuppression. This can be associated with significant morbidity to the patient. A brief table describing some of the adverse effects and risks associated with this therapy is shown in Fig. 4. These risks must be weighed heavily when considering the potential for this type of reconstruction.

Immunosuppression has been associated with an increased risk of cancer recurrences, as well as the

Fig. 4 Adverse effects and risks associated with immunosuppression

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development of new cancers. For this reason, a history of active cancer or a potential risk for recurrent tumor is an absolute contraindication at this time for allograft procedures. These are reserved within the context of experimental protocols at this juncture.

Rejection, both acute and chronic, is a serious potential complication of any transplant procedure. This can result in organ loss. With the face, this potential outcome is magnified in significance. Appropriate salvage plans and backup protocols are essential steps in planning such a procedure. To date, there have been no faces lost due to rejection in compliant patients. Having said this, acute rejection, however, is a common phenomenon reported with multiple events in every single case in the literature. Fortunately, these episodes have been managed by short-term immunomodulation in all of the cases with relative ease [2, 6–9, 10].

Ethical Considerations

The medical risks associated with transplantation highlight one of the unique factors that must be considered in weighing the appropriateness of the procedure [11]. At this time, face transplants remain experimental surgery, and ethical considerations have been and should remain paramount in the development of any protocol for this surgery. A full discussion of the ethical implications of this procedure warrants its own chapter and is beyond the scope of this discussion. Having said that, the general principles of autonomy, beneficence, and non-maleficence, which form the foundations of the ethics of medicine, should be considered in every case. The concept of potentially life-threatening complications for a reconstructive surgery is a reality with this procedure. The benefits must be enough to outweigh this risk.

Therefore, the surgery should only be considered in individuals who have suffered a loss in their quality of life that warrants the acceptance of these risks. Proper evaluation of the capacity of the recipient to make this decision, their understanding of the risks and benefits, and their potential compliance with lifelong therapy is critical.

Beyond this difficult decision of risk/benefit, there are other considerations unique to facial transplantation. The concept of identity is at the heart of this procedure. Does the recipient lose their identity? Does the donor transfer their identity? Or is it both? The preclinical data with cadaver work as well as the clinical experience have shown this to be less problematic than initially predicted. While full face transplants share similarities to the donor, variations in skeletal structure and facial shape result in the recipient's transplanted face assuming a composite appearance that is neither donor nor recipient in origin.

The recipient's identification with and connection to their new face is a transformation in and of itself. Fortunately, this has not been a difficult adjustment for patients to make. In their own words, they have lost their old face and now are so disfigured that they feel "inhuman." The goal in these patients is not to restore their pre-injury face, but merely to have a face that allows them to return to human socialization. In many respects, this represents a paradigm shift for the reconstructive surgeon whose holy grail has always been the restoration of the pre-injury state. Facial transplantation is not restoration—it is replacement.

Surgical Indications for Facial Transplantation

Facial transplantation should be reserved for individuals with significant mid-facial neuromuscular injuries. Complete absence or loss of the function of the orbicularis oris

muscle along with a concurrent complete nasal defect is probably the minimal indication for considering allograft-based reconstructions [5]. Defects can extend beyond these limits to include eyelids and the full face, but the minimum deficit requiring allograft approaches is the central neuromuscular segment of the mid-face. The inclusion criteria at present include ballistic and physical trauma (i.e., burns) exclusively. The potential risk of the loss of cancer surveillance under immunosuppression precludes post surgical ablation of malignancy as a potential indication.

Allograft Design and Classification Scheme

Numerous allograft procurement protocols have been described in the literature. At this relative stage of infancy of this procedure, the majority of allografts have been tailored to the defects of the individual patients. At the time of writing of this chapter, only 25 facial transplantation procedures have been performed worldwide. Despite the variability in the cases, some common themes are present across all of the procedures. The facial artery alone provides the arterial inflow in the majority (18 of 25 cases), and in a few cases, the external carotid artery has been used. Angiographic studies, as well as clinical experience, have shown that the facial artery is sufficient to supply a full face transplant including the maxilla. The palate, although primarily supplied by palatine vessels from the internal maxillary system, can easily be perfused via oral mucosal vascular networks from the facial artery [12]. The venous outflow has been traditionally based on the common facial

veins, as well as the external jugular venous system. Some surgeons have chosen to use the internal jugular vein, but it is clear that the common facial vein is adequate for the venous drainage of the inferior facial structures. The cross circulation in the face is so well established that vascular reconstitution of one side of the face alone will allow for perfusion of both sides across the midline.

The depth of the allograft harvest must be below the plane of the facial musculature and the facial nerve. In order to achieve a neuromuscular reconstruction, the facial nerve must be carefully dissected and preserved. Individual facial nerve branches are isolated, and a sequential and segmental series of neurotaphies are performed.

A simplistic way to understand the various facial procurement protocols is to consider them as a combination of traditional surgical approaches. For example, the combination of a bicoronal flap, a LeFort 3 level osteotomy, and bilateral superficial parotidectomy plan elevation is a full face procurement. The bi-coronal flap, which is a component of all facial procurement protocols, and the other surgical approaches used preserve allograft vascularity and nerve function. Using a combination of surgical approaches, a blueprint for the allograft procurement appropriate for the patient's facial defects can be created. The procurement procedures are not novel surgical techniques, but merely a new perspective on the use of accepted surgical approaches.

Clinical Experience

At this early point in the history of facial transplantation, the worldwide clinical experience is too limited to have

Fig. 5 Pre-operative clinical presentation of the first U.S. facial transplant recipient

any significant data to support its long-term efficacy. The largest reported clinical series remains only three patients. Thus, the reports remain an exercise in proof of concept and anecdotal experience. My personal involvement in the field of facial transplantation has involved two cases. I was the primary surgeon for the first case in the United States (case #4 worldwide) involving a patient with a shotgun injury to the mid-face. I was also a part of the surgical team for a second patient who suffered an animal attack injury resulting in a total facial avulsion and underwent a full face transplant (case #21 worldwide). The evolution of this surgical procedure during the time between these two cases illustrates the rapidly advancing nature of this field.

Case One

Indication

At the time of her facial transplantation, this patient was a 46-year-old woman who had underwent 23 prior reconstructive procedures, including four failed free flaps performed by an outside group of surgeons. Her pre-operative clinical presentation is shown in Fig. 5. She continued to have significant disfigurement and functional limitation after these procedures and therefore was seen for evaluation by the multi-disciplinary Cleveland Clinic Face Transplant Team (established in 2004 following institutional review board approval).

The entire mid-face of this patient was functionally absent or surgically altered. The extent of the defect included a complete absence of any nasal or septal structure. This defect had been previously managed by soft tissue coverage using a paramedian forehead flap. There was also an absence of maxilla, zygomatic arches, and inferior orbital rims. Additionally, scar contracture in the mid-face and the prior flap coverage eliminated a nasal passageway, rendering the patient anosmic and an obligate mouth breather. The absence of any mimetic musculature in the mid-face left her with a functional bilateral facial paralysis and significant oral incompetence. The tissues in this region were residual components of her prior reconstructions and were non-functional. Another consequence of her extensive prior surgeries was scarring and fibrosis in the soft tissue of the neck and the resultant depletion of suitable recipient vessels.

Anatomical Design and Flap Procurement

Based upon the specific anatomical requirements of this patient, the technical design of the donor flap was

undertaken once the exhaustive pre-transplant work-up was finalized. This pre-transplant assessment included evaluations from the departments of transplant surgery, transplant psychiatry, and bioethics. The complex nature of the patient's skeletal loss presented the unique challenge of incorporating vascularized maxilla into the transplanted face. The design of the donor facial soft tissue and skin envelope incorporated the entire cheek subunit, the entire nose, and the entire upper lip. The flap was planned as a full-thickness flap including the buccal mucosa of the mid-face. In the lower third of the face, where the patient had existing viable tissue, the allograft flap was procured in the sub-plastysmal plane with incorporation of both the parotid and portions of the submandibular glands for safe preservation of the neurovascular pedicles. This design intentionally incorporated redundant glandular tissue, which will need to be removed in a planned revision procedure in the future. The donor's hypoglossal nerves were also included as a motor nerve graft to bridge the gap between the recipient's mid-face division branch of the facial nerve and the donor facial nerve trunk created by the redundant parotid gland tissue. Since the inflow axons are only mid-

Fig. 6 Illustration of the facial transplant allograft—**a** schematic, **b** actual specimen

Fig. 7 Surgical steps for the facial transplantation in a–d

face in origin, this neurorrhaphy would reduce potential synkinesis and inappropriate facial movement. An illustration of the transplant allograft is shown in Fig. 6. The surgical steps are outlined in Fig. 7.

Outcomes

Late post-operative outcomes are shown in Fig. 8. At the time of the writing of this chapter, the patient is 4 years post-operative. The incorporation of the allograft has been complete with no graft loss. She has recovered facial nerve function and facial sensation. She has had restoration of all of her mid-facial functions lost following her injury, including smiling and laughing. The esthetic outcomes are limited by her pre-existing eyelid trauma that has not been

addressed by the transplant, as well as the outcomes of the transplant itself. She has redundant parotid tissue that needs to be removed, and her facial nerve has been asymmetric with greater functional recovery on her left side. Despite these limitations, she is able to integrate herself into social environments almost seamlessly.

Case Two

Indication

At the time of her facial transplant, the patient was a 46-year-old woman who was the victim of a chimpanzee attack that resulted in a near total facial avulsion. She was

Fig. 8 Late post-operative outcomes (~4 years post-facial transplantation) demonstrating recovery of facial nerve and mid-facial function

Fig. 9 Pre-operative initial clinical presentation of case two

initially managed with debridement and wound care to stabilize her infected wounds. At initial presentation, she was in a medically induced coma from which she was unarousable. Approximately 1 month following her injury, she awoke and regained normal cognitive function.

Subsequently, she underwent interval reconstruction with local advancement flaps, an anterolateral thigh free flap, and rib cartilage graft to temporize her condition. Her initial presentation and repair are shown in Fig. 9.

Anatomical Design and Flap Procurement

The extent of injury in this case required the utilization of a full facial transplant. While the prior procedure was planned with the approach of defining a unique and novel surgical approach to the exact defect, the design of this transplant was based upon traditional surgical approaches. The design of this flap is shown in Fig. 10. The allograft is a composite of a bicoronal flap, bilateral parotid dissections, LeFort 3 level osteotomies, and oral mucosal release. The neck plane is in the standard sub-platysmal plane with dissection of the facial arterial and venous vascular system. The superficial parotid glands are removed in this case eliminating the need for revision parotid surgery.

With full facial transfer, isolation of individual facial nerve branches is a critical step. Neural coaptation was performed at distal locations to prevent synkinesis and improve selective motor function. Patients with injury to the facial nerve proximal to the pes anserinus are poor candidates for full facial transplantations for this reason.

Fig. 10 Full face procurement—bicoronal flap, a Lefort 3 level osteotomy and bilateral superficial parotidectomy plane elevation

Outcomes

The immediate post-operative outcome of this patient is shown in Fig. 11. She is now almost 2 year post-transplantation with full graft take and functional recovery. She has restoration of functional facial movement bilaterally, although her facial nerve function remains slightly paretic. She has been able to return to society, in spite of her blindness and loss of hands that remain significant residual disabilities.

Conclusions

Despite the relative infancy of the field of facial transplantation, the optimism for its role in facial reconstruction remains high. This has been the consequence of both the successful early outcomes and the complex nature of the problem that the surgery addresses. We currently have no means to repair complex neuromuscular injuries of the face. While free flaps have offered us an effective tool to transfer tissue, we remain unable to functionally connect

Fig. 11 Immediate post-operative outcome

the transferred tissues to the brain to create a functional reconstruction. The gracilis free flap reconstruction begins to scratch the surface of this issue but it is clearly a limited indication for a single function. In massive injuries, there are still no great options. It is in this futility that the strongest arguments in favor of facial transplantation can be made.

Over the first 25 cases, the technique has improved and this trend should continue as more cases are performed and long-term follow-up of early cases becomes possible. The true success of this operation remains an unanswered question at this stage, but the early outlook remains promising.

Compliance with Ethics Guidelines

Conflict of Interest Daniel Alam declares that he have no conflict of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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