Perspectives

Ethical Considerations of Whole-Eye Transplantation

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ABSTRACT

Whole eye transplantation (WET) remains experimental. Long presumed impossible, recent scientific advances regarding WET suggest that it may become a clinical reality. However, the ethical implications of WET as an experimental therapeutic strategy remain largely unexplored. This article evaluates the ethical considerations surrounding WET as an emerging experimental treatment for vision loss. A thorough review of published literature pertaining to WET was performed; ethical issues were identified during review of the articles.

INTRODUCTION

As of 2008, reports indicate that 37 million people worldwide suffered from irreversible vision loss, with 20 percent, or 7.4 million, having vision consisting of only light perception or worse.[1] The majority of irreversible blindness is due to age-related diseases such as macular degeneration, diabetic retinopathy and glaucoma,[2] followed closely by trauma and ocular tumors.[3] The irreversible nature of this vision loss largely results from permanent optic nerve damage. Damaged axons of the retinal ganglion cells (RGCs)—the output neurons from the retina that form the optic nerve—do not regain their function following insult. Whole-eye transplantation (WET) could potentially provide a blind recipient with viable RGCs capable of regeneration and reintegration, as well as the optical system necessary for capturing and transmitting images to the visual cortex.

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WET is not a novel concept for the treatment of vision loss, but it is only now that it is becoming technically feasible and emerging as a potential experimental therapy. As early as the 1920s, Koppanyi and Kolmer demonstrated that the eyes of various cold- and warmblooded vertebrates could be removed and transplanted back into the eye socket, and that certain functions of the eyeball were retained.[4] Not until 1977 did an advisory council for the National Eye Institute (NEI) form and call for a ''limited and thoughtful laboratory effort'' in the area of eye transplantation. The NEI council stated, ''any effort to transplant a mammalian eye is doomed to failure by the ganglion cell axon's inability to withstand cutting, by the difficulty of insuring adequate circulation of blood to the transplanted eye during or shortly after the operation, and lastly by immune rejection of foreign tissue,'' yet, they concluded, ''the subject [of eye transplantation] is of such overriding clinical importance that it merits research attention.''[5]

Substantial progress has been made in the field of optic nerve regeneration since the NEI council originally made these statements back in 1977. Over the last 40 years, significant advancements have been made to the extent that WET is now nearing emergence as an experimental therapy for treating irreversible vision loss.[6] The intent of this article, however, is not to provide an overview of the advances that have made the possibility of WET clinically feasible in the future, but rather to begin to explore key ethical issues surrounding WET and its implementation as an experimental therapeutic strategy.

Over the past decade, vascularized composite allotransplantation (VCA) of the hand and face has emerged as a reconstructive option for devastating tissue loss in some patients.[7] This is a novel specialty, and more than 200 VCA procedures have been performed around the world, including 95 hand and 30 face transplants. When the first articles on the ethics of facial transplantation were published in the early 2000s, the first face transplant had not yet been performed. Lantieri, a French surgeon who was one of the pioneers of face transplantation, had postulated that the triad of anatomic dysfunction, patient characteristics, and team experience would dictate whether facial transplantation could be done ethically.[8] We are witnessing a similar evolution of the ethical questions surrounding WET, as seen in the early developmental phases of facial transplantation. Just like facial transplantation, WET is not to be considered as lifesaving, but as life-enhancing. Unlike facial transplantation, however, WET has the potential to restore vision, and, as such, to return what was previously thought to be a permanently lost sensation. Given these concerns, it is important to begin to explore the ethical considerations surrounding WET as an emerging experimental treatment for vision loss.

METHODS

A review of articles available pertaining to WET was performed and the resulting ethical concerns are discussed in terms of standard ethical principles.

RESULTS

Autonomy

To date, there have been no WET procedures performed, so it remains uncertain whether acute or chronic graft rejection and graft versus host disease (GVHD) episodes will occur at a frequency comparable with that of solid organ transplantation. Expected infections with this type of procedure can be inferred from other types of transplantation and include Candida, cytomegalovirus, Epstein-Barr virus (EBV), Herpes simplex, Herpes zoster, Molluscum contagiosum, Pseudomonas aeruginosa, and staphylococcal infection. Cancers are of great concern following any transplantation. For example, following facial transplantation, there have been three reported cases of cancer in the literature: one case of cervical dysplasia requiring hysterectomy, and two cases of post-transplant lymphoproliferative disorder; one was HIV related, and the other resulted in death.[9]

Organ donation has created ethical concerns regarding the privacy of patients, donors, and their families. The recognition and identity of donors and patients following WET would not seem to be of concern, but may be when WET and facial transplantation could be combined. Aversion to ocular donation for use in corneal transplantation procedures has already been documented.[10] WET is likely to be viewed by the public as an extension of, or analogous to, corneal transplantation, and thus may not be met with the same degree of sensationalism as facial transplantation, but the possibility does exist for the combination of WET and facial transplantation procedures. Public education and awareness of WET as a novel procedure are critical to assure the privacy of patients.

Providing ongoing support and psychiatric treatment for organ donors and recipients, and support for their families, is required to assure the long-term continuity of care and reflects a care team's concern for the best interest of patients and donors. While some donor families may choose to meet organ re-

cipients to explain their decision to donate the eyes of their family member, members of the care team must strive to preserve the confidentiality of all patients, donors, and family members.

The dignity of donors and their family members also must be protected. Respecting the integrity of a donor's body is an important value for the surgical team, and prostheses should be made to restore the deceased donor's body after recovery, should there be a desire for open casket viewing. The surgical team should spend time with the donor's family to help prepare them for the high likelihood of seeing the recipient in the news following the initial WET procedures.

Beneficence and Nonmaleficence

The need for, and subsequent consequences of, long-term immunosuppression is an important concern, due to the risk of infection, cardiovascular effects, and the possibility of kidney damage. The risk of post-transplant lymphoproliferative disorder (PTLD) is a real concern. For reference, there have been three cases of lymphoma reported in vascularized composite allotransplantation (VCA), two faces and one lower extremity.[11] One face transplant patient and one lower extremity transplant patient have succumbed to this fatal condition.[12] With two cases of PTLD in face transplant alone, this is a 7.7 percent risk so far in the first 26 recipients.[13] Albeit small numbers of VCA have been performed to allow meaningful extrapolation with solid organ PTLD risk, it is important to consider the statistics.

By comparison, according to the U.S. Organ Procurement Transplant Network/United Network for Organ Sharing database, the incidence of PTLD between 1999 and 2008 are as follows: for kidney recipients, 1.58 percent; for liver recipients, 2.44 percent; for heart recipients, 2.24 percent; for lung recipients, 5.72 percent. The incidence of other post-transplant malignancies, such as Kaposi's sarcoma, and bronchial and lung cancer in solid organ recipients is higher than it is for the general population of 55 to 59 year olds.[14] It remains to be seen if ocular transplantation carries with it the same risks as other organ systems, but it may be equivalent, if not decreased, given the immune-privileged nature of the anterior chamber of the eye.

The acceptance of risk varies depending on the procedure proposed, but the acceptance of risks of immunosuppression could change, if the incidence of PTLD or post-transplant malignancies rises substantially.[15] An aspect of nonmaleficence that must be discussed is that a donor may never have considered eye donation as a possibility, so there cannot be an assumption of his or her implied consent. As the eye is visible, unique, and highly personal, the donor's family must be involved in the consent process, as there should be no unwilling participants. In this complex process, the process of procurement itself will need to be protected, as bad publicity can result in a drop in the rate of solid organ donation, with the consequent deaths of those on waiting lists.

Losee and colleagues addressed the selection of patients as a way mitigate medical risk through a standardized evaluation to limit the incidence of PTLD and noncompliance with immunosuppression, which they found to be highest, respectively, in children and adolescents.[16] Ruling out patients who have pre-existing medical problems (history of malignancies, HIV infection, traumatic brain injury), or co-existing medical problems (diabetes or heart disease), or family history of diseases that could impact outcomes (amyloidosis, congenital bone diseases, familial neuropathies or malignancies) may reduce overall risk. In addition, an assessment of adherence may minimize postoperative harm while acknowledging that the rate of non-adherence across 147 studies that assessed various organ systems was 22.6 cases per 100 patients per year.[17]

Justice

Age considerations may be important to WET in so far as younger patients may gain the greatest benefit due to higher propensity for nerve regeneration. But adolescents also have historically high rates of non-adherence with immunosuppression in solid organ transplantation and higher rates of PTLD that could affect survival.[18]

Decisions regarding the selection of patients for solid organ transplant must include considerations of justice, but must also consider the lifesaving nature of the procedures. Rating scales such as the Stanford Integrated Psychosocial Assessment for Transplantation instrument (SIPAT) incorporate considerations of justice. These rating scales standardize psychosocial selection processes for transplantation, and may have prognostic value regarding readmission rates for rejection, infection, and mortality. Scores that are greater than 42 on the SIPAT are thought to be incompatible with successful transplantation; however, measures may be undertaken to improve the score, retain the candidate for transplant, and improve the outcomes of recipients.[19] Similar systems that will be perhaps even more stringent will need to be constructed and investigated if WET becomes an established therapy.

CONCLUSION

Whole eye transplantation (WET) is highly experimental. While it was long thought to be impossible, recent scientific advances suggest that WET may soon be possible. The ethical implications regarding WET as a therapeutic strategy remain largely unexplored. This article evaluates the ethical considerations surrounding WET as an emerging experimental treatment for vision loss. Loss of vision has devastating impacts on a person's overall health and psychosocial well-being. The gravity of functional impairments and the inability to reconstruct the eye justify the exploration of WET as a potential therapeutic strategy.

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NOTES

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