

Guest Editorial

LARYNGOTRACHEAL TRANSPLANTATION

Transplanting tissue or organ to save the life of a patient was in the dreams of medical practitioners for a long time. The world famous horror novel of nineteenth century 'Dracula' by Irish novelist Bram Stoker, whose brother Thornely Stoker was a neurosurgeon in Dublin, contains detailed description of blood transfusion attempted by Dr Van Helsing to save Lucy Westenra, the unfortunate victim of count Dracula. This was written well before Karl Landsteiner described the ABO blood groups in 1901 and long before Alexander S Weiner found out the Rh groups in 1936. So, there was no question of Van Helsing doing any grouping and cross matching to prevent the dreaded transfusion reactions. During the Second World War, Gibson and Medawar¹ found out the problem of graft rejection, when they attempted skin grafting for big burns in pilots. They found that skin graft taken from the same individual (autograft) survived, while that taken from another individual (allograft or homograft) was rejected. Obviously, a graft from a different species (xenograft) had no chance of survival. Later physicians found out that graft from an identical twin (isograft) was not rejected. This landmark discovery culminated in the first successful organ transplant, when Murray et al² successfully transplanted a kidney from an identical twin in 1955 in Boston. Medawar's³ work in rabbits and in mice (1944) led to similar studies in human beings and human leukocyte antigen (HLA) system was discovered. This naturally led to various methods by which the immune system could be manipulated so that rejection became less.



Once the scientists got a clue about modifying the immune system so as to prevent the rejection of the transplanted organ, surgeons started transplanting more and more organs. The most exciting of them was the first successful heart transplant by Barnard in 1967.⁴ The highly challenging liver transplant became a reality in early 1980s. Bone marrow, pancreas, lung and small intestine followed. Recently, face and hand, two very sensitive organs have been successfully transplanted. So, it was only natural, that surgeons started thinking about transplanting the larynx.

The first attempt to transplant the entire larynx was done by Professor Paul Kluyskens⁵ in Belgium in 1969. But, his patient died 4 and half months after the surgery. Marshall Strome⁶ et al successfully transplanted the larynx in 1998 in Cleveland, USA. Timothy Heidler, a 40-year-old man, who had badly damaged his larynx in a motor cycle accident was the recipient. Thirteen years after the surgery, he is hale, hearty and healthy. Very recently, Birchall⁷ et al transplanted the larynx to Ms Brenda Jensen, whose larynx was damaged beyond repair by multiple intubations and an accidental rough extubation. Tintinago⁸ reported a series of laryngotracheal transplantations in 2007.

Issues in Laryngeal Transplantations

Donor

Laryngeal transplantation for obvious reasons is from cadaver only. Patients who died from intracranial hemorrhage, head injury or severe road traffic accidents were the ideal laryngeal donors. Smokers and persons with infectious diseases are avoided. Blood group and HLA matching are mandatory. It is also important that the donor was intubated for not more than 48 hours prior to death. The harvested larynx should be transplanted within 20 hours to reduce the chance of ischemia.⁶

Recipient

Even though, there are umpteen numbers of patients who underwent total laryngectomy, only a minority are candidates for laryngeal transplantation as of now. This is because of the fact that, vast majority of them lost their larynx due to surgery for cancer. Obviously, immunosuppression administered after the transplantation increases the risk of recurrence of cancer. So, the ideal candidate would be a person who lost his or her larynx secondary to trauma, where the damage was irreparable.

Avoiding Rejection

In all organ transplantations, three types of rejection can occur. Hyperacute rejection which occurs in few hours is due to preformed antibodies in a sensitized patient. Acute rejection due to cell mediated immunity happens in few days to few weeks time. Chronic rejection occurring over a period of months to years is most probably due to humeral antibodies. Rejection is prevented by tissue typing and reducing the immune response. For laryngeal transplantation, both blood group matching and

HLA typing is necessary. Immune response reduction is by steroids, azathioprine and cyclosporine. More recently, drugs like tacrolimus, sirolimus and mycophenolate mofetil are being used.

Surgical Technique

Larynx along with upper tracheal rings, thyroid and parathyroid glands is transplanted. Ideally, internal jugular veins with the attached middle thyroid veins and superior thyroid arteries are anastomosed to the available nearby major vein and artery. Superior and recurrent laryngeal nerves are anastomosed to the corresponding nerves on both sides.

Postoperative Period

Voice is the first of the major functions to return. It was of great interest to note that the recipient had a voice similar to his or her voice rather than that of the donor. This consolidates the current concept about the importance of resonating structures in determining the individuality of the voice and vocal cords being the mere vibrators. Swallowing was the second function to recover. Tintinago secured an adequate airway at the glottic level by performing a Kashima posterior cordotomy.

Controversies

The antagonists of laryngeal transplantation argue that larynx is not an essential organ like heart, liver or kidney.⁹ They also opine that most important dysfunction of aphonia can be corrected to a great extent by esophageal speech, electronic larynx or tracheoesophageal puncture and voice prosthesis. The risk and expense of lifelong immunosuppression is the other major concern. Larynx being a highly physiologically dynamic organ poses the problem of securing the effective neurological function. Ideally after successful transplantation, the vocal cords should abduct during inspiration and adduct during phonation and swallowing. Even with the best of microsurgical techniques, this is most often not possible.

Tracheal Transplantation

Tintinago¹⁰ described the first successful tracheal transplantation in 2002 for a patient in whom 95% of trachea was lost. Cadaver trachea was transplanted with inferior thyroid artery as the major blood supply.

Future of Laryngotracheal Transplantation

The reported success of the few laryngeal transplants is likely to cause a renewed interest especially in the field of laryngeal transplantation. The incidence of road traffic accidents is on the increase in many countries. Hence, there will be many more cases of mutilating damages to voice boxes. With the advent of less toxic immunosuppressants, it is quite likely that more and more laryngeal transplants will be carried out in the future. Even in cases of laryngeal cancer, transplants are not out of place. Many authorities have actually suggested that laryngeal transplantation can be done in patients who are disease free at the end of 5 years. So far the laryngeal transplant attempts have been done only in American continents and Europe. It is quite surprising to note that, in view of the great advances by the Japanese laryngologists, no laryngeal transplant has been done in Asia yet.

Successful stem cell transplant of trachea by Elliot et al¹¹ recently has generated great enthusiasm and hope in the field of airway stenosis. This was done in a child in whom a very long segment of trachea was stenotic and where all the other corrective surgical techniques were tried and failed. The child was transplanted with donor trachea laced with the stem cells from the patient himself. The great advantage of this procedure is the fact that there is no need for expensive and potentially toxic lifelong immune suppression. Most probably, this is going to be the future in the treatment of severe tracheal dysfunction. However, it is too early to tell whether this will be equally successful in more complex organs like larynx.

Just like any other organ transplantation, laryngeal transplantation also is to be done after thorough and meticulous planning. Since it is a cadaver transplant, ethical issues like medical guidelines for declaration of brain death and right of the individual and the family to dispose the organ have to be considered. Better immune modulation and improved microsurgical techniques are definitely going to improve the long-term results. The ultimate goal of a near normally functioning transplanted larynx may not be a distant dream anymore. The recent advances in the stem cell technology, no doubt will help many unfortunate patients, who have major tracheal dysfunction.

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