CHAPTER 25

COMPOSITE TISSUE ALLOTRANSPLANTATION

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I. INTRODUCTION

A. Also referred to as Vascularized Composite Allotransplantation (VCA) or Composite Tissue Allograft (CTA)
B. Allograft (graft from cadaveric donor) composed of different tissue types (e.g. skin, muscle, bone, nerves, vessels)
C. Introduced for major reconstruction of tissue defects from surgical excision of tumors, traumatic injury and congenital malformations
   1. Option for limb replacement and reconstruction of other non-reconstructible tissue defects including facial, abdominal wall and others
D. Couples the principles of microsurgical reconstruction with those of human organ transplantation
E. Goal: improve function, quality of life, integration with society

II. IMMUNOGENICITY

A. CTA are histologically heterogeneous, composed of different tissue types including skin, fat, muscle, nerves, lymph nodes, blood vessels, bone, cartilage, ligaments, and bone marrow
B. Each tissue has different antigenicity
   1. Skin most antigenic, likely owing to dendritic cell population and antigen variety
   2. CTA graft is not the sum of immunogenicity of its different components
   3. Whole limb allograft elicits a less intense immune response than does allografts of each of the individual components
C. CTA elicit a stronger immune response as compared to solid organ transplants
D. Split tolerance phenomenon: simultaneous tolerance to one tissue and rejection of another from the same donor

III. DEVELOPMENT

A. Rapidly progressing field
B. > 150 composite tissue allograft worldwide to date
C. An estimated 7 million people per year in the United States could benefit from composite tissue allotransplantation
D. Online international registry of hand and composite tissue transplantation: https://www.handregistry.com/
IV. HISTORY

A. 348 AD: 'The legend of the black leg' / Legend of Saints Cosmos and Damien
   1. Tale of twin brothers Cosmas and Damian who replaced the diseased leg of a man with that of a recently deceased person
B. 1954: first successful human organ isograft, a kidney donated between identical twins; USA (Joseph E. Murray, John P. Merrill, and J. Hartwell Harrison)
C. 1964: first case of hand CTA, failed due to rejection after 3 weeks; Ecuador (Robert Gilbert)
D. 1990s: progress in immunosuppression → composite tissue renaissance
E. 1998: first successful hand CTA; France (Jean-Michel Dubernard)
F. 2000: first successful bilateral hand CTA; France (Jean-Michel Dubernard)
G. 2005: first successful partial face transplantation; France (Devauchelle, Dubernard)

V. TYPES OF CTA PERFORMED TO DATE

A. Hand / upper extremity
   1. Most common transplant
      a. First 4 successful cases:
         i. Right hand – transplanted in Lyon, France, on September 23, 1998
         ii. Left hand – transplanted in Louisville, KY on January 23, 1999
         iii. 2 right hands – transplanted to two individuals in Guangzhou, China, on September 21, 1999
   2. > 80 upper limbs reported in 2015
B. Partial or total face
   1. first partial face transplant in 2005 in France
   2. > 25 cases reported in 2015
C. Abdominal wall
   1. Typically, in the setting of abdominal multi-organ transplant
D. Knee
E. Larynx
F. Flexor tendon apparatus
G. Peripheral nerve
H. Tongue
I. Trachea
J. Esophagus
K. Scalp
   1. In the setting of active malignancy, and with simultaneous solid organ transplantation
L. Penis
M. Uterus
   1. with the first successful pregnancy following uterus transplant in 2015 in a Swedish woman
VI. ADVANTAGES

A. Replace “like with like”
B. An option when standard reconstructive options are exhausted or autologous tissues are not available
C. Can achieve structural, functional, esthetic, and psychological result
D. Avoidance of any donor site morbidity
E. Good functional outcomes
   1. for example, for hand transplants:
      a. Sensibility recovered 6-12 months
      b. Motor function allows return to most daily activities (eating, driving, grasping objects, riding a bicycle or a motorbike, shaving, using the telephone, and writing)
F. Majority of patients are satisfied and report improved quality of life

VII. DISADVANTAGES / LIMITING FACTORS

A. Need to determine appropriate indications
B. No consensus on which physical defects justify reconstruction with CTA

VIII. DONOR-RECIPIENT MATCHING CRITERIA

A. ABO
B. Graft size
C. Skin pigmentation
D. Age
E. Gender

IX. DETERMINATION OF ORGAN ALLOCATION

A. Patient level
   1. complex decision making
   2. important discussion with recipient regarding donor and recipient skin pigmentation, age mismatch, and gender
B. Society level
   1. no current policy
   2. societal values variable on the benefits and risks of CTA
C. Need for indefinite immunosuppressive
   1. Always at risk for rejection
   2. Predominant limiting factor: side effects of immunosuppression
D. Opportunistic infections
E. Drug toxicity
1. Metabolic disorders
2. Nephrotoxicity
3. End-organ damage
F. Malignancies
   1. Heightened antigenicity of composite tissues → difficult to develop an effective yet nontoxic immunosuppressive protocol
G. Uncertain long term outcomes
   1. Limited long term experience
   2. Unknown if CTA will undergo chronic rejection leading to diminished functional capacities

X. FUTURE DIRECTIONS

A. Results of the first clinical cases are encouraging, but still controversial.
   1. Significant progress in the last 2 decades
   2. Novel immunosuppression and medication regimens may improve motor and sensory function, and decrease episodes of rejection
   3. Novel donor-specific tolerance regimens (i.e., simultaneous bone marrow transplantation to induce bone marrow chimerism and central tolerance)
B. Increasing application for a wider group of patients as surgery is streamlined, tolerance regimens are perfected, and outcomes are improved.

REFERENCES


