Role of Stem Cells in Breast Reconstruction After Mastectomy

Essay

Submitted for partial fulfillment of Master Degree ***in General surgery***

By:

Ramy Sultan Saad Sultan

(M. B., B.Ch)

Supervised by

Prof. Dr. Mahmoud Ahmed ElShafey
Professor of General Surgery
Faculty of Medicine, Ain Shams University

Dr. Abdel Rahman Mohamed Abdel Aal
Lecturer of Plastic & Reconstructive surgery
Faculty of Medicine, Ain Shams University

Dr. Ahmed Samy Mohamed
Lecturer of General Surgery
Faculty of Medicine, Ain shams University

Faculty of Medicine
Ain Shams University
2014

Acknowledgement

First of all, all gratitude is due to ***God*** *almighty for blessing this work, until it has reached its end, as a part of his generous help, throughout my life.*

Really I can hardly find the words to express my gratitude to ***Prof. Dr. Mahmoud Ahmed ElShafey,*** *Professor of General Surgery faculty of medicine, Ain Shams University, for his supervision, continuous help, encouragement throughout this work and tremendous effort he has done in the meticulous revision of the whole work. It is a great honor to work under his guidance and supervision.*

I would like also to express my sincere appreciation and gratitude to ***Dr. Abdel Rahman Mohamed Abdel Aal*** *Lecturer of Plastic & Reconstructive surgery, faculty of medicine , Ain Shams University, for his continuous unlimited help, unlimited patience and close supervision throughout the entire work.*

I feel deeply thankful to ***Dr. Ahmed Samy Mohamed*** *Lecturer of General Surgery, faculty of medicine, Ain Shams University, for his continuous directions and support throughout the whole work.*

Last but not least, I dedicate this work to my family, whom without their sincere emotional support, pushing me forward this work would not have ever been completed.

Ramy Sultan Saad Sultan

Contents

List of Abbreviations

ADSCs	:	Adipose-derived stem cells.
ASPS	:	American Society of Plastic Surgeons
CAL	:	Cell-Assisted Lipotransfer
DIEP	:	Deep inferior epigastric artery perforator
ESCs	:	Embryonic stem cells
FDA	:	Food and Drug Administration
HSCs	:	Hematopoietic stem cells
LDMF	:	Latissimus dorsi muscle flap
MSCs	:	Mesenchymal stem cells
NAC	:	Nipple-areola complex
NH	:	Non-hemolytic
PBSCs	:	Peripheral blood stem cells
SIEA	:	Superficial Inferior Epigastric Artery Flap
SVF	:	Stromal vascular fraction
TRAM	:	Transverse rectus abdominis myocutaneous
TUG	:	Transverse upper gracilis flap
UCBs	:	Umbilical cord blood

List of Figures

List of Figures (Cont.)

List of Figures (Cont.)

Introduction

Breast reconstruction after mastectomy has evolved over the last century to be an integral component in the therapy for patients with breast cancer. Breast reconstruction originally was designed to reduce postmastectomy complications and to correct chest wall deformity, but its value has been recognized to extend past this limited view of use. The goals for patients undergoing reconstruction are to correct the anatomic defect and to restore form and breast symmetry. The surgical options for breast reconstruction involve the use of endoprostheses (implants), autogenous tissue transfers, or a combination of both. ***(Bostwick and Carlson, 1997)***

The goal of breast reconstruction is to recreate symmetric natural-appearing breasts while preserving patient safety and quality of life. Many techniques exist for breast reconstruction, but rarely do they produce true symmetry with the contralateral breast.

The safety of the patient is essential and always should remain the primary concern in reconstructive procedures. These procedures should be tailored to the individual patient, taking into account the ultimate aesthetic outcome and the impact the reconstruction may have on the patient's lifestyle. ***(Gui et al., 2008)***.

Tremendous advances in breast reconstruction have occurred in the past 3 decades. Although breast reconstruction with tissue expanders and implants remains the most common form of reconstruction, autogenous tissue has grown more popular. In the past decade, breast reconstruction has advanced because of the popularity of skin-sparing mastectomy. When immediate reconstruction is performed following a skin-sparing mastectomy in a nonirradiated breast, the demands on the plastic surgeon are reduced and the postoperative result is improved cosmesis. ***(Kinoshita et al., 2013).***

Today, a new era dawns on the field. The potential of stem cells therapies and regenerative medicine is both provocative and powerful, offering the distinct possibility of eventually repairing or replacing tissues damaged from disease, including certain cancers. The major body of scientific work performed in tens of thousands of laboratories worldwide is slowly giving way to clinical translation.***(Atala, 2012)***

By definition, a stem cell is characterized by its ability to self-renew and its ability to differentiate along multiple lineage pathways. This tremendous feature of the stem cells can be a major turn in the future of clinical practice of breast reconstruction, delivering the desired safety, good cosmetic results and minimal morbidities of other sites of the body that is the major drawbacks of the currently used techniques ***(Gimble, 2003)***

Aim of the Work

To study the implications of stem cells and possible methods of integration of this rising field in the reconstructive approaches in breast surgeries following mastectomy.

Breast Anatomy

The breast is located within the superficial fascia on the anterior thoracic wall. It consists of 15to20 lobes of glandular tissue of the tubuloalveolar type. Each lobe is supported by fibrous connective tissue that forms a framework. Adipose tissue fills the space between the lobes. ***(Cowie et al., 1980).***

Although a distinct capsule around the components of the breast is not present, subcutaneous connective tissue surrounds the gland and extends as a septum between the lobes and lobules providing support for the glandular elements. The deep layer of the superficial fascia that lies on the posterior surface of the breast rests on the pectoral fascia of the thoracic wall. A distinct space, the retromammary bursa, can be identified anatomically on the posterior aspect of the breast between the deep layer of the superficial fascia and the deep investing fascia of the pectoralis major and contiguous muscles of the thoracic wall (Fig.1)**. *(Romrell et al., 2004).***

Fig. (1): Diagrammatic sagittal section through the non lactating female breast and anterior thoracic wall ***(Romrell et al., 2004)*.**

Anterior fibrous processes, the suspensory ligaments of Cooper pass from the septa that divide the lobules of the breast to insert into the skin. The posterior aspect of the breast is separated from the deep, or the investing fascia of the pectoralis major muscle by a space filled with loose areolar tissue, the retromammary space or bursa. The existence of the retromammary space and the suspensory ligaments of Cooper allow the breast to move freely against the thoracic wall. The space between the well defined fascial planes of the breast and pectoralis major is easily identified by the surgeon removing a breast ***(Jatoi et al.,2006).***

Connective tissue thickenings, called posterior suspensory ligaments, extend from the deep surface of the breast to the deep pectoral fascia ***(Jatoi et al., 2006).***

Extent and locations:

The mature female breast extends inferiorly from the level of the second or third rib to the inframammary fold, which is at about the level of the sixth or seventh rib, and laterally from the lateral border of the sternum to the anterior edge of the latissimus dorsi muscle or the anterior or midaxillary line. The deep or posterior surface of the breast rests on portions of the deep investing fasciae of the pectoralis major, serratus anterior, and external abdominal oblique muscles and the upper extent of the rectus sheath. The axillary tail (of Spence) of the breast extends into the anterior axillary fold. The upper half of the breast, and particularly the upper outer quadrant, contains more glandular tissue than does the remainder of the breast ***(Krontiras and Bland, 2006).***

Vascular Supply

Arterial Supply

The arterial supply of the breast forms a rich anastomotic plexus. With considerable variation, the breast is supplied with blood from three sources: the internal thoracic artery, the branches of the axillary artery and the intercostal arteries ***(Morehead ,1982)*** **(Fig.2).**

- ***Internal Thoracic Artery (or internal mammary):***

The internal thoracic artery produces the largest vessel supplying the breast, and the internal thoracic branches supply most of the blood to the breast. The internal thoracic artery is a branch of the subclavian artery; it courses parallel with the lateral border of the sternum behind the transversus thoracis muscles. From the internal thoracic artery, perforating branches pass through the intercostal muscles of the first six interspaces and the pectoralis major muscle to supply the medial half of the breast and surrounding skin **.** Perforating arteries pierce the thoracic wall adjacent to the sternal edge in the 1^{st}-4^{th} intercostals spaces. Typically these arteries descend laterally toward the nipple-areola complex so that most of the arterial supply arises above the level of the nipple. Therefore, radial incisions in the upper half of the breast are less likely to injure the major arterial supply than are the transverse incisions. Morehead stated that the inferior parts of the breast below the level of the nipple are almost free of major vessels ***(Morehead,1982).***

- ***Branches of the Axillary Artery:***

The axillary vasculature supplies the lateral portion of the breast. Branches from the axillary artery to the breast include the small supreme thoracic artery, the pectoral

branches of the thoracoacromial artery, the lateral thoracic artery, and the subscapular artery,which gives twigs of supply to lateral aspect of the breast, the lateral thoracic artery is the most important of these vessels ***(Morehead, 1982).***

- ***Intercostal Arteries:***

In addition to the vasculature described above, the lateral half of the breast may also receive branches of the 3rd, 4th, and 5th intercostal arteries. Small branches of the intercostal arteries in the 2nd, 3^{rd}, and 4^{th} spaces pass to the overlying breast tissue. Only about 18% of breasts are supplied by all three of these sources. Branches from the internal thoracic artery are the only ones always present to some degree. In most breasts, there are free anastomosis between the arteries supplying the breast; occasionally all three arterial sources remain *separate* ***(Maliniac,1943).***