Autoimmune Diseases and the Microchimerism Legacy of Pregnancy

Essay

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Nesreen Micheal

Contents

List of Abbreviations

Abbrev.

AD ……..Alzheimer’s disease.

ANA……Antibodies against the nucleus.

APCs……Antigen presenting cells.

BBB……Blood brain barrier.

bp……..Basal plate.

CHB……..CongenItal heart block.

CTL……Cyto toxic T lymphocyte.

dcSSc……..Diffuse cutanuos systemic sclerosis.

dsDNA……Double stranded DNA.

EGFP……..Enhanced green fluorescent protein.

FISH……Fluorescent in-situ hybridisation.

FFPE……Formalin-fixed paraffin-embedded .

Fetal Mc…Fetal microchimerism.

Fmsc……Fetal mesenchymal stem cells.

GD……..Gestational days.

GvHD…….Graft versus host disease .

HEV……High endothelial venule.

HLA……Human leukocyte antigen.

HvG……..Host-vs-graft .

JDM …… Juvenile dermatomyositis .

lcSSc……..Limited cutanuos systemic sclerosis.

LTx……Liver transplantation.

MDCs……Myeloid dendritic cells.

MHC……The major histo competability complex .

Maternal Mc……Maternal microchimerism .

NIMA……. Non-inherited maternal antigen.

NIPA……. Non-inherited Paternal antigen.

NK…….. Natural killer.

NLS…… Neonatal lupus syndrome .

P0…….. The day of parturition.

PAPC……. pregnancy associated progenitor cells.

PBMC……. peripheral blood mononuclear cell.

PBC…… Primary biliary cirrhosis.

PCR…….. Polymerase chain reaction.

RA…….. Rheumatoid arthritis.

RTx……. Renal transplantation.

SCID……Severe combined immunodeficiency.

SLE……..Systemic lupus erythematosus.

SRY……Sex-determining region Y protein.

SSc…… Systemic sclerosis.

TA-Mc……Transfusion associated microchimerism.

T1D……Type 1 diabetes.

Th……T helper.

Th2…….T helper2 .

TRALI…….Transfusion-related acute lung injury.

WPB……Whole peripheral blood.

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Introduction

Introduction

The presence of a small population of cells or DNA in one individual that derives from another genetically distinct person is referred to as microchimerism (Mc); this process may occur in course of pregnancy from mother to fetus, and vice versa. The clinical similarities between some features of autoimmune diseases and the chronic graft versus host disease (GvHD), the increased incidence of autoimmune diseases observed in women after childbearing age, and the long-term persistence of Mc have raised the hypothesis that Mc could be involved in the pathogenesis of autoimmune disease ***(Turco and Bambra, 2004).***

Fetal microchimerism (fetal Mc) has been hypothesized as a potential pathogenic mechanism for systemic sclerosis (SSc). This hypothesis was based on the clinical similarities between SSc and GvHD and the identification of microchimeric cells in affected SSc tissues ***(Sawaya et al., 2004).*** Recent investigations have demonstrated microchimeric cells in the clinically uninvolved tissues from patients with systemic sclerosis ***(Jimenez and Artlett, 2005).***

Several studies have linked fetal Mc with autoimmune thyroid disease, which occurs frequently in women, particularly postpartum. Greater frequency of male

DNA has been found in thyroid tissue of women with Hashimoto's disease compared to nodular goiter and also in Graves' disease compared to controls with adenoma. Recently, using a quantitative PCR assay, fetal Mc was detected in 8 of 21 thyroid samples from women with Hashimoto's disease compared to 0 of 17 healthy thyroid glands ***(Adams and Nelson, 2008).***

Fetal cells have been found in women with systemic lupus erythematosus (SLE), both in the blood and a target organ, the kidney, suggesting that they may be involved in the pathogenesis of the disease ***(Stevens, 2006).***

Neonatal lupus syndrome-congenital heart block (NLS-CHB) is an acquired autoimmune disease in which maternal autoantibodies are necessary but not sufficient for disease. Maternal myocardial cells have been found in the hearts of patients with NLS-CHB, suggesting that maternal microchimerism may also play a role ***(Stevens et al., 2004).***

Type 1 diabetes (T1D) is an autoimmune disease that primarily affects children and young adults ***(Nelson et al., 2007)***, found that levels of circulating maternal Mc were higher in T1D patients than unaffected siblings as well as unrelated healthy individuals and chimeric islet β cells were observed in pancreatic autopsy specimens of patients with T1D.

Aim of the Work

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To highlight the legacy of microchimerism from the perspective of autoimmune diseases.

Chapter (1)

Microchimerism

Microchimerism

Definition:

Microchimerism is defined as the presence of a small population of cells or DNA in one individual that derives from another genetically distinct person ***(Knippen, 2011).***

Root of the word Chimera:

In Greek mythology, a chimera is a fire-breathing monster with the head of a lion, the body of a goat, and the tail of a serpent (Figure 1).

In biology, a chimera is an organism consisting of tissues whose cells derived from two or more genetic sources. An apple tree, for example, can include grafts that enable it to produce a variety of apple types. In humans, such genetic mosaics reflect specific, intimate circumstances. What is special about chimera is its almost indestructible. A creature is able to compensate for some of its shortcomings, because it not only possesses its own strength, but also has the added strength of another. That was the idea when it entered medical terminology; an experimental animal or a human that accepts another genetic make-up, tolerates it and becomes its permanent host ***(Bettens et al., 2005).***

The phenomenon is termed Mc because a one-cell population is typically much smaller than the other Mc can be defined as less than 1% of foreign cells present in an individual ***(Pujal and Gallardo, 2008).***

Figure (1): The Chimera of Arezzo

The Chimera of Arezzo is a bronze statue found in Arezzo, Italy, in 1553 (Archeological museum in Firenze). Chimera is a mythic three-head.

(Galofré and Davies, 2007).