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Overview Of Immunocompromised Patients

Graduation Project

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أَعُوذُ بِاللَّهِ مِنَ الشَّيْطَانِ الرَّجِيمِ

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

وَقُلْ رَبِّ زِدْنِي عِلْمًا

صدَقَ الله العَظِيم

سورة طه جزء من الآية ﴿١١٤﴾

Dedication

Everything I am ,

Or ever will be , I owe it to my parents

My success because of them

To you MOM and DAD

And this is just the beginning

&

To my biggest supporters ,

Who keep saying “ I am proud of you “

In my failures before my success .

To my brothers

Introduction

Among patients admitted to the hospital with an infection, some may have some form of immunodeficiency. Immunodeficiency is divided into primary, acquired and iatrogenic immunodeficiency. Primary immunodeficiency disorders (PIDs) comprise a group of genetically heterogeneous, primarily childhood disorders that affect certain components of the innate and adaptive immune systems and lead to serious complications. [1,2] The most common immunodeficiency is acquired after birth and is uncertainly obtainable to a genetic basis. [3].

Primary Immunodeficiency (PID)

PID disorders are inherited disorders, sometimes caused by mutations in a single gene or, more commonly, by an unknown genetic predisposition combined with environmental factors. Although some PIDs are diagnosed in infancy or childhood, many are diagnosed later in life. PID is classified according to which part of the immune system is dysfunctional. [4]

Examples of Primary Immunodeficiency Diseases

- B cell immunodeficiency (adaptive) – B cells are one of two key cell types in the adaptive immune system. Their main job is to produce antibodies. These are proteins that bind to microbes, making it easier for other immune cells to recognize and kill them. Mutations in the genes that control B cells lead to loss of antibody production. These patients are at risk for severe recurrent bacterial infections.

- T cell immunodeficiency (adaptive) – T cells are the second of two key cell types in the adaptive immune system. One job of T cells is to activate B cells and pass on details about the microbe's identity so that the B cells can make the correct antibodies. Some T cells are also directly involved in killing microbes. T cells also provide signals to activate other cells in the immune system. Mutations in the genes that control T cells can cause T cells to decline or not function properly. This reduces their ability to kill and often leads to problems with B cell function. Thus, T-cell immunodeficiency often results in combined immunodeficiency (CID), in which both T-cell and B-cell functions are defective. Some forms of CID are more serious than others.
- Severe combined immune deficiencies (SCID) (adaptive) – SCID disorders are very rare but extremely serious. In SCID patients there is often a complete lack of T cells and variable numbers of B cells, resulting in little-to-no immune function, so even a minor infection can be deadly. SCID patients are usually diagnosed in the first year of life with symptoms such as recurrent infections and failure to thrive.
- Phagocyte disorders (innate) - phagocytes include many white blood cells of the innate immune system, and these cells patrol the body eating any pathogens they come across. Mutations typically affect the ability of certain phagocytes to eat and destroy pathogens effectively. These patients have largely functional immune systems but certain bacterial and fungal infections can cause very serious harm or death.
- Complement defects (innate) – complement defects are some of the rarest of all the PIDs, and account for less than 1% of diagnosed cases. Complement is the name given to specific proteins in the blood that help immune cells clear infection. Some

deficiencies in the complement system can result in the development of autoimmune conditions such as systemic lupus erythematosus and rheumatoid arthritis (please see our autoimmune briefing for more information). Patients who lack certain complement proteins are highly susceptible to meningitis.[4]

Types of Primary Immune Deficiency Diseases

There are more than 200 different forms of primary immune deficiency diseases (PIDDs). NIAID conducts research across all PIDDs as well as among the individual diseases that make up this broad category. The following are some of the individual PIDDs that NIAID is currently studying.

- **Autoimmune lymphoproliferative syndrome (ALPS) :** is a rare immune disorder that can cause numerous autoimmune problems, such as low levels of red blood cells, clot-forming platelets, and infection-fighting white blood cells. These problems can increase the risk of infection and hemorrhage.
- **Chronic Granulomatous Disease (CGD):** occurs when white blood cells called phagocytes are unable to kill certain bacteria and fungi, making people highly susceptible to some bacterial and fungal infections. Mutations in one of five different genes can cause this disease.
- **Congenital neutropenia syndromes:** are a group of disorders present from birth that are characterized by low levels of neutrophils, a type of white blood cell necessary for fighting infections.
- **X-Linked Agammaglobulinemia (XLA):** is caused by an inability to produce B cells or immunoglobulins (antibodies),

which are made by B cells. People with XLA develop frequent infections of the ears, throat, lungs, and sinuses.

Secondary immunodeficiency (SID)

IDs are more common than PIDs and are the result of a primary illness, such as HIV, or other external factor such as malnutrition or some drug regimens. Most SIDs can be resolved by treating the primary condition.

There are many potential causes of SID but the most common examples are blood or bone marrow disorders, drugs (medicines) and treatment for cancer. Some cancers can be responsible for SID, too.

The main medicines that cause problems are those that target the immune system, including immunosuppressant drugs, 'biologics' and chemotherapy. These medicines may have been used in the treatment of conditions such as rheumatoid arthritis, multiple sclerosis, inflammatory bowel disease and psoriasis, and of blood and lymph node cancers in particular.

There are other medicines that are recognised as causing specific complications with the immune system and these effects are not directly related to the way the drug works. For example, some anti-epileptic drugs can cause antibody deficiency.[5]

Causes of Secondary Immunodeficiency Disorders

- Radiation or chemotherapy, which can lead to a secondary immunodeficiency disorder known as neutropenia
- Chronic disease
- Severe burns
- Infections due to human immunodeficiency virus (HIV) can result in acquired immune deficiency syndrome (AIDS)

- Leukemia, a cancer that begins in the cells of the bone marrow that can lead to hypogammaglobulinemia—a type of secondary immunodeficiency
- Malnutrition, which affects up to 50% of populations in underdeveloped countries and leaves people vulnerable to respiratory infections and diarrhea
- Drugs or medications. Certain medications that suppress the immune system in people with autoimmune disorders can increase the risk of infections.
- Chronic infections. Chronic infections, such as acquired immune deficiency syndrome (AIDS), caused by HIV infection, can lead to several secondary immunodeficiency disorders. In this condition, the virus targets white blood cells of your body—which fight infections and bacteria—while multiplying. Over time, the number of white blood cells decreases, leaving the body vulnerable to a variety of diseases.

Examples of secondary immunodeficiency disorders

Treatment-related

Corticosteroids are used to treat a variety of diseases because of their anti-inflammatory and immunosuppressive properties (6,7). They have many effects on innate and acquired immunity.

- Impair disable dealing of neutrophils and monocytes to sites of inflammation
- inhibit macrophage and neutrophil phagocytic and microbicidal function (8,9).
- They inhibit the production of almost all known cytokines (10). markedly reduce the number of circulating dendritic and T cells

- affect antigen presentation by impairing the effector functions of macrophages and dendritic cells (11-14).

Chronic infections

There are a number of chronic infections which can lead to SID disorders, the most common of which is acquired immune deficiency syndrome (AIDS), resulting from HIV infection. The virus attacks CD4+ T cells, a type of white blood cell that plays a critical role in preventing infection, and gradually depletes their numbers. Once the T cell count is less than 200 cells per ml of blood, symptoms of AIDS begin to manifest and the patient is at high risk of recurrent infections that will eventually lead to death. Anti-viral therapies, such as the HAART regimen (Highly Active Antiretroviral Therapy), allow the T cell population a chance to recover and resume normal function.

Hematologic Malignancies

In addition to the effects of chemotherapy, cancers can predispose the host to develop infections if the cancer spreads to the bone marrow and/or lymph nodes, and thereby reduces the number of normal hematopoeitic cells. This is particularly true for lymphoid malignancies, such as leukemia and lymphoma.

Chronic lymphocytic leukemia (CLL) CLL patients are at increased risk for infection because the leukemia cells can replace normal lymphocytes in the bone marrow and lymph nodes, and because of adverse effects of the drugs used to treat the disease. Defects of humoral immunity are common, and the problem appears to be exacerbated by the use of rituximab (15).

Metabolic Diseases

Diabetes mellitus Both type 1 and type 2 diabetes mellitus can increase an individual's risk for infections because of reduced blood supply and denervation of peripheral tissues. It also appears that poor glycemic control is associated with impaired neutrophil function. Neutrophils from diabetics have decreased expression of adhesion molecules, as well as impaired in vitro adhesion and chemotaxis (16).

What Are the Symptoms of Immunodeficiency Disorders?

The most common immunodeficiency symptoms are:

- Diarrhea
- Pneumonia
- Sinus infections
- Ear Infections
- Inflammation of internal organs
- Colds
- Pinkeye
- Digestive issues, like diminished hunger and nausea
- Yeast infections

Symptoms vary for each immunodeficiency disorder, which can be either acute (sudden and short term) or chronic (occurring over a long period).

Risk factors

- People who have a family history of primary immunodeficiency disorders have a higher risk for developing primary disorders themselves.
- Anything that weakens the immune system can lead to a secondary immunodeficiency disorder. For example, exposure to body fluids

infected with HIV or organ removal and replacement can both be causes.

- Aging can also weaken your immune system. As you age, some of the organs that produce or process white blood cells shrink and become less efficient.
- Proteins are important for your immunity. Not enough protein in your diet can weaken your immune system.
- The body also produces proteins when you sleep that help the body fight infection. For this reason, lack of sleep can reduce immune defenses.

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