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Med Surg Assignment (NSC 306)
1. Primary immunodeficiency disorders are:
-Wiscott-Aldrich syndrome.
-Severe combined immunodeficiency disease (SCID)
-Ataxia-telangectasia.
-Chronic granulomatous disease.
-Complement deficiencies.
A-**Wiskott–Aldrich syndrome (WAS):** It is a rare X-linked recessive disease characterized by eczema, thrombocytopenia (low platelet count), immune deficiency, and bloody diarrhea (secondary to the thrombocytopenia. The WAS-related disorders of X-linked thrombocytopenia (XLT) and X-linked congenital neutropenia (XLN) may present similar but less severe symptoms and are caused by mutations of the same gene.
Signs and symptoms:
Petechiae, bruising, nose bleeds,

bloody diarrhea, eczema, bacterial infections,autoimmune disorder, cancers (mainly lymphoma and leukemia), elevated eosinophil counts.

Pathophysiology: The microthrombocytes seen in WAS patients have only been observed in one other condition, ARPC1B deficiency. In both conditions the defective platelets are thought to be removed from circulation by the spleen and/or liver, leading to low platelet counts. WAS patients have increased susceptibility to infections, particularly of the ears and sinuses, and this immune deficiency has been linked to decreased antibody production and the inability of immune T cells to effectively combat infection.

Treatment: Treatment of Wiskott–Aldrich syndrome is currently based on correcting symptoms. Aspirin and other nonsteroidal anti-inflammatory drugs should be avoided, since

these may interfere with platelet function which is already compromised. A protective helmet can protect children from bleeding into the brain which could result from head injuries. For severely low platelet counts, patients may require platelet transfusions or removal of the spleen. For patients with frequent infections, intravenous immunoglobulins (IVIG) can be given to boost the immune system. Anemia from bleeding may require iron supplementation or blood transfusion. As WAS is primarily a disorder of the blood-forming tissues, a hematopoietic stem cell transplant, accomplished through an umbilical cord blood or bone marrow transplant offers the only current hope of cure. This may be recommended for patients with HLA-identical donors, matched sibling donors, or even in cases of incomplete matches if the patient is age 5 or under.

B**-Severe combined immunodeficiency (SCID):** It is a rare genetic disorder characterized by the disturbed development of functional T cells and B cells caused by numerous genetic mutations that result in differing clinical presentations. SCID involves defective antibody response due to either direct involvement with B lymphocytes or through improper B lymphocyte activation due to non-functional T-helper cells. Consequently, both "arms" (B cells and T cells) of the adaptive immune system are impaired due to a defect in one of several possible genes. SCID is the most severe form of primary immunodeficiencies, and there are now at least nine different known genes in which mutations lead to a form of SCID. It is also known as the bubble boy disease and bubble baby disease because its victims are extremely vulnerable to infectious diseases

and some of them, such as David Vetter, have become famous for living in a sterile environment. SCID is the result of an immune system so highly compromised that it is considered almost absent.

Treatment: Bone marrow transplantation and prophylaxis against infection.

C-Ataxia–telangiectasia (AT or A–T): Also referred to as ataxia–telangiectasia syndrome or Louis–Bar syndrome, is a rare, neurodegenerative, autosomal recessive disease causing severe disability. Ataxia refers to poor coordination and telangiectasia to small dilated blood vessels, both of which are hallmarks of the disease.

Signs and symptoms: -Ataxia (difficulty with control of movement) that is apparent early but worsens in school to pre-teen years

-Oculomotor apraxia (difficulty with coordination of head and eye

movement when shifting gaze from one place to the next).
-Telangiectasia (dilated blood vessels) over the white (sclera) of the eyes, making them appear bloodshot.
-Dysarthria (slurred, slow, or distorted speech sounds)
-Diabetes in adolescence or later.
-Premature changes in hair and skin.
Pathophysiology: A–T has been described as a genome instability syndrome, a DNA repair disorder and a DNA damage response (DDR) syndrome. ATM, the gene responsible for this multi-system disorder, encodes a protein of the same name which coordinates the cellular response to DNA double strand breaks (DSBs). Radiation therapy, chemotherapy that acts like radiation (radiomimetic drugs) and certain biochemical processes and metabolites can cause DSBs. When these breaks occur, ATM stops the cell from making new

DNA (cell cycle arrest) and recruits and activates other proteins to repair the damage. Thus, ATM allows the cell to repair its DNA before the completion of cell division. If DNA damage is too severe, ATM will mediate the process of programmed cell death (apoptosis) to eliminate the cell and prevent genomic instability.

D**- Chronic granulomatous disease (CGD**): (also known as Bridges–Good syndrome, chronic granulomatous disorder, and Quie syndrom) is a diverse group of hereditary diseases in which certain cells of the immune system have difficulty forming the reactive oxygen compounds (most importantly the superoxide radical due to defective phagocyte NADPH oxidase) used to kill certain ingested pathogens. This leads to the formation of granulomata in many organs. CGD affects about 1 in 200,000 people in the United States, with

about 20 new cases diagnosed each year.

Signs and symptoms: pneumonia,abscesses of the skin, tissues, and organs, septic arthritis, osteomyelitis, bacteremia/fungemia, superficial skin infections such as cellulitis or impetigo.

Pathophysiology: Phagocytes (i.e. neutrophils and macrophages) require an enzyme to produce reactive oxygen species to destroy bacteria after they are ingested (phagocytosis), a process known as the respiratory burst. This enzyme is termed "phagocyte NADPH oxidase" (PHOX). This enzyme oxidizes NADPH and reduces molecular oxygen to produce superoxide anions, a reactive oxygen species. Superoxide is then disproportionated into peroxide and molecular oxygen by superoxide dismutase. Finally, peroxide is used by myeloperoxidase to oxidize

chloride ions into hypochlorite (the active component of bleach), which is toxic to bacteria. Thus, NADPH oxidase is critical for phagocyte killing of bacteria through reactive oxygen species.
Treatment: -Antibiotics: Physicians often prescribe the antibiotic trimethoprim-sulfamethoxazole to prevent bacterial infections. This drug also has the benefit of sparing the normal bacteria of the digestive tract. Fungal infection is commonly prevented with itraconazole, although a newer drug of the same type called voriconazole may be more effective. The use of this drug for this purpose is still under scientific investigation.
-Immunomodulation: Interferon, in the form of interferon gamma-1b (Actimmune) is approved by the Food and Drug Administration for the prevention of infection in CGD. It has been shown to reduce infections in

CGD patients by 70% and to decrease their severity. Although its exact mechanism is still not entirely understood, it has the ability to give CGD patients more immune function and therefore, greater ability to fight off infections.

-Hematopoietic stem cell transplantation (HSCT): Hematopoietic stem cell transplantation from a matched donor is curative although not without significant risk.

E**- Complement deficiency:** is an immunodeficiency of absent or suboptimal functioning of one of the complement system proteins. Because there are redundancies in the immune system, many complement disorders are never diagnosed, some studies estimated that less than 10% are identified. Hypocomplementemia may be used more generally to refer to decreased complement levels while secondary complement disorder means

decreased complement levels that are not directly due to a genetic cause but secondary to another medical condition.
Sign and symptoms: Recurring infection, Auto-immune disorders, Glomerulonephritis, Joint problems (manifestation), Lung function (MBL variant alleles), Angioedema, Dermatomyositis, Vasculitis, Anaphylactoid purpura.
Treatment: Immunosuppressive therapy..

2. Secondary immunodeficiency disorders are:
-Cancers of the immune system like leukemia.
-Multiple myelona (cancer of primary cells, which products antibodies).
A**- Leukemia,** also spelled leukaemia, is a group of blood cancers that usually begin in the bone marrow and result in high numbers of abnormal blood cells. These blood cells are not fully

developed and are called blasts or leukemia cells. Symptoms may include bleeding and bruising, feeling tired, fever, and an increased risk of infections. These symptoms occur due to a lack of normal blood cells. Diagnosis is typically made by blood tests or bone marrow biopsy.

Signs and symptoms: Bleeding, bruising, feeling tired, fever, increased risk of infections.

Treatment: Chemotherapy, radiation therapy, targeted therapy, bone marrow transplant, supportive care.

B-**Multiple myelona** (cancer of primary cells, which products antibodies): Multiple myeloma (MM), also known as plasma cell myeloma and simple myeloma, is a cancer of plasma cells, a type of white blood cell that normally produces antibodies. Often, no symptoms are noticed initially. As it progresses, bone pain, bleeding, frequent infections, and

anemia may occur. Complications may include amyloidosis.
Signs and symptoms: Bone pain, bleeding, frequent infections, anemia.
Treatment: Steroids, chemotherapy, thalidomide, stem cell transplant, bisphosphonates, radiation therapy.
Pathophysiology: B lymphocytes start in the bone marrow and move to the lymph nodes. As they progress, they mature and display different proteins on their cell surfaces. When they are activated to secrete antibodies, they are known as plasma cells. Multiple myeloma develops in B lymphocytes after they have left the part of the lymph node known as the germinal center. The normal cell line most closely associated with MM cells is generally taken to be either an activated memory B cell or the precursor to plasma cells, the plasmablast.
The immune system keeps the

proliferation of B cells and the secretion of antibodies under tight control. When chromosomes and genes are damaged, often through rearrangement, this control is lost. Often, a promoter gene moves (or translocates) to a chromosome, where it stimulates an antibody gene to overproduction. A chromosomal translocation between the immunoglobulin heavy chain gene (on chromosome 14, locus q32) and an oncogene (often 11q13, 4p16.3, 6p21, 16q23 and 20q11) is frequently observed in people with multiple myeloma. This mutation results in dysregulation of the oncogene which is thought to be an important initiating event in the pathogenesis of myeloma. The result is a proliferation of a plasma cell clone and genomic instability that leads to further mutations and translocations. The chromosome 14 abnormality is observed in about 50% of all cases of myeloma. Deletion of

(parts of) chromosome 13 is also observed in about 50% of cases. Production of cytokines (especially IL-6) by the plasma cells causes much of their localised damage, such as osteoporosis, and creates a microenvironment in which the malignant cells thrive. Angiogenesis (the generation of new blood vessels) is increased.. The produced antibodies are deposited in various organs, leading to kidney failure, polyneuropathy, and various other myeloma-associated symptoms.