**Sheet no: 2**

**Refer to slide no: included in slide #1**

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***Rheumatoid arthritis***

Rheumatoid arthritis: we hear about it more but it’s not the most common. Osteoarthritis is the most common one. Rheumatoid arthritis is a chronic inflammatory disease (the main pathogenesis is inflammation, chronic course of inflammation)

-The cause of inflammation in rheumatoid arthritis is an autoimmunity, therefore it’s an autoimmune disease (no tolerance to self-antigens).

-Our immune system is divided into, 1- humoral immunity (B-lymphocytes, which produce and release antibodies), 2-cell mediated immunity (T-lymphocytes)

-the main autoimmune pathogenesis in rheumatoid arthritis is the cell mediated immunity (through T-lymphocytes, specifically T-helper cells also called CD4 T-lymphocytes)

-these cells (T-helper cells) recognize self-antigens and start producing specific substances against them, these substances are called cytokines, they mainly produce interferon gamma, that activates macrophages found in different tissues, macrophages when triggered they produce cytokines as well, mainly interleukin 1, and **tumor necrotic factor** (this is very important factor, antibodies against it is now been used for the management of rheumatoid arthritis).

-there are many type of cells that are related to the pathogenesis in rheumatoid arthritis, on the top of which are the synoviocytes (cells lining the synovial membrane ), fibroblasts ,macrophages, plasma cells( antibody production, humoral immunity)are also involved.

- pathogenesis in rheumatoid arthritis is not only cellular, rather humoral immunity contributes as well, antibodies bind to self-antigens whether in the blood or those normally found in the joints, Ag-Ab complex (also called immune complex) accumulate in the joints causing destruction and activation of many WBCs in there, as well as cytokines secretion causing inflammation, and so destruction keeps in progression if not managed properly.

-fibroblasts ,synovial cells ,macrophages and many other cells in the joints undergo proliferation during the inflammatory process ,therefore the number of cells in the joints increase ,increasing the symptoms of the disease, and so ,progression in the joints’ destruction results .

-rheumatoid arthritis mainly affects people between the 2nd-4th decade (20-40 years of age) .

-unlike rheumatoid arthritis, primary osteoarthritis affects people of old ages.

-rheumatoid arthritis is a systemic autoimmune disease , it affects the muscles, skin, blood vessels ,heart and many other tissues in our body , not only the joints ( it affects the whole body, it’s a systemic multiorgan disease ).

-it mainly affects females (3X more than males).

-rheumatoid factor being measured in people with rheumatoid arthritis, indicates the disease process , though it’s not found in all patients ,and when found not necessarily positive in all rheumatoid arthritis patients.

-IgM and IgA react with IgG **MISTAKINGLY** forming immune complex depositions causing rheumatoid arthritis.

-inflammation causes the activation of chondrocytes, synovial cells and fibroblasts.

-pathology is the study of the etiology, mechanism of the disease, and morphology (gross morphology and microscopic morphology) and the clinical picture of the patients.

-etiology can be due to: 1- genetic factors: mutations and genetic variations among people , for instance some people are more susceptible of having specific diseases more than others due to the genetic variation, 2-environmental factors , a-infections for example, might cause changes in self-antigens converting them to infectious agents ,so antibodies will be produced and released against them causing the disease ,b-smoking, is another environmental agent that might cause the previously mentioned changes .

- Enzymatic modification: which is the change in self –antigens, so that antibodies will be produced against them causing an autoimmune disease.

-there are many types of T-cells, each of which produces different type of cytokines.

-hyperplasia occur in chondrocytes ,fibroblasts, and synovial cells due to the inflammatory process, these cells produces enzymes that break the matrix of the joints , some of which are , collagenase ,strmelysin,andelastase.

- pannus formation: destruction of the bone and cartilage causing, lesions in the joints , accumulation of inflammatory cells and clotting materials .

-rheumatoid arthritis is an autoimmune chronic inflammatory diseases, since its chronic the tissue repair or renewal process will be in the form of fibrosis, so fibrotic bands will form and fill the space between the bones of the joint, then these bands will be converted to bone by ossification, and fusion between the bones of the joint will occur, this is called ankylosis. (This is different from the osteoarthritis where no fusion occur)

-rheumatoid arthritis mainly occur in small joints, and symmetrical in both sides of the body, symmetrical arthritis (in both right and left side of the body).

-in rheumatoid arthritis distal interphalangeal joints are spared, spines are spared as well especially the lumber ones.

-Constitutional symptoms: weakness, malaise, and low-grade fever caused by the release of IL-1, TNF by macrophages.

-chronic, remitting-relapsing course

-Treatment: immuno-suppressive therapy, including biologic agents that antagonize TNF.

-inflammation in rheumatoid arthritis extends to other soft tissues and ligaments around the joint, causing many deformities and disabilities in the limbs.

- amyliodosis is the deposition of abnormally folded proteins , causing tissue destruction.

- Primary amyloidosis: Alzheimer’s disease, malignant multiple myeloma (in plasma cells, where an increase in the light chains of Igs occur).

- Secondary amyloidosis is the major complication in chronic inflammatory processes.

**- Infectious arthritis**:

hematogenous dissemination(from the blood to the bones of the joints).

Can be from the surrounding area to the bones of the joints .

Trauma of the joints

Orthopedic surgeries

Usually occurs in one joint.

-infectious arthritis is a critical case, for its acute, severe and has the ability to destroy surrounding muscles.

**-Suppurative arthritis**:

Haemophilus influenza it’s the main cause in children <2 yrs.

S. aureusis it’s the main cause in older children and adults.

Gonococcus (gonoccocal arthritis) is prevalent in older adolescents (sexually active late adolescents), and young adults (mainly females).

Patients with sickle cell disease are prone to Salmonella infection at any age.

-immunodeficiency of certain complement proteins (C5, C6, and C7) , disseminated gonococcal infections and hence arthritis ( this immunodeficiency increases the susceptibility of having gonoccocal arthritis).

**-Classic presentation:**

Acute, severe, localized illness in the infected region, severe swelling, pain and fever.

Leukocytosis and elevated ESR (erythrocyte sedimentation rate) along with CRT(C-reactive proteins).

-Gonoccocal arthritis takes more time to progress ( subacute course ).

-90% of non-gonococcal arthritis is in a single joint.

- Most common in the knee, hip, shoulder, elbow, wrist, and StC joints (in descending order).

-Joint aspiration, when we take a sample of the fluid from the infected joint, we will find a purulent fluid “pus” containing neutrophils, bacteria, and necrotic cells (culture +ve).

Treatment: antibiotics and joint aspiration.