Lecture - 2

PG Sem-3
Dec 10
Unit V

Immunodeficiency diseases

Natural Immunity Diseases -

Chediak - Higashi disease - It is an neutrophil dysfunction inherited disease, commonly found in man, cattle, Beige mice etc. In this disease the melanin granules of skin become unusually enlarged giving pale brown colour. The neutrophils reveal presence of large dark granules within the lobed nucleus These granules become enlarged and fragile which rupture spontaneously causing histopathological changes in the tissues.

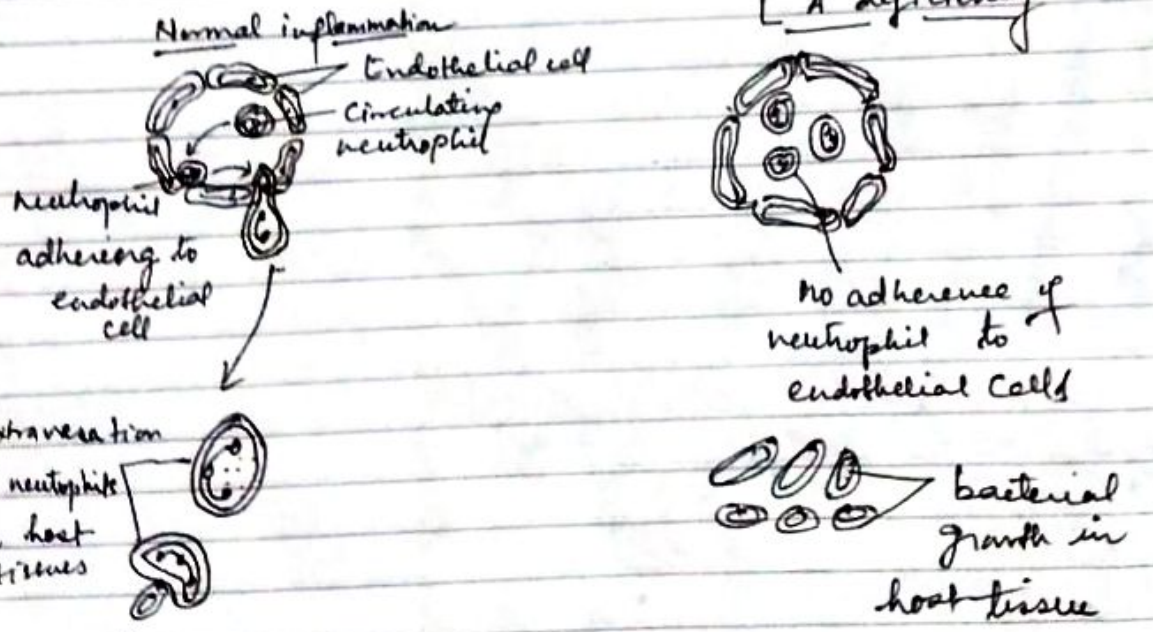
The lysosomes of patients of this disease become deficient in enzyme elastase and cathepsin - G due to which they suffer from pyogenic infections and which may lead to their death. Patients also suffer from myeloperoxidase deficiency, which makes them susceptible to fungal infection Candida albicans. In these patients there is also a deficiency of NK cells and cytotoxic CD8 cells lymphocytes, Because of low level of neutral proteases, the neutrophil show reduced intracellular Killing. The most severe kind of inherited abnormality is of non expression of CD11b, CD18 and CD11 complement receptors that cause leukocyte adherence deficiency (LAD) The LAD in turn result into deficiency of chemoattractants especially for complement receptors, CD, 11b and CD18 are member of B_2 integrin family necessary for chemotactic responsiveness mediated by chemoattractin Complement protein 5a. It induces binding of neutrophils to endothelial cells. In LAD patients the neutrophil neither bind with complement

receptors nor they can enter into tissues to kill antigens by mounting inflammatory reactions but neutrophil bind to particles coated with immune complex C_3b or to the ligand already bound to endothelial cells causing leukocyte adherence deficiency causing recurrent microbial infection in patients.

Complement Protein deficiency – The deficiency of complement protein and complement inhibitors are because of defective expression of genes. Deficiency of complement components results in increased susceptibility to infections. Deficiency of complement proteins C_1 results in non recognition of microorganisms. In hereditary angioedema inhibitor of active C1 component is lacking which causes non inflammatory edema mediated by vasoactive complement protein C_2. In humans deficiency of factor I inhibitor and C3b inactivator results in serious infection of pyogenic bacteria. During alternative complement pathway each erythrocyte is bombarded by about 1000 C_3b complement protein generated during formation of C3 convertase. The deficiency of two inhibitors of the MAC complex (Membrane attack) called homologous restriction factor (HRF) along with CD59 cause complements mediated lysis of RBC. HRF and CD59 bind to the RBC membrane by C8 through glycosyl phosphatidylinositol anchors and thus preventing the unfolding the first C_9 converted molecule as essential for membrane insertion. In Paroxysmal

hemoglobinuria (PHN) the above anchor are not synthesized and hence there is no binding of ARF and CD59 to membrane and hence no complement mediated lysis of erythrocytes takes place.

The deficiency of classical pathway complementary proteins C1q, C1r C1s, C4 and C2 results in high incidence of systemic lupus erythematous disease (SLE). Although permanent deficiency of C5, C6, C7, C8 and C9 complement proteins may lead healthy life but are susceptible to neisserial gonorrhoea and neisseria meningitis infections. Deficiency of the regulatory proteins of complement component causes autoimmune diseases.



A.

fig - Normal inflammatory conditions neutrophil adhere endothelial cells, extravasate into tissue and phagocytose bacteria

B. LA deficiency - No adherence of neutrophil to endothelial cell and no killing of bacteria in tissue facilitating bacterial growth

Phagocytosis of bacteria by neutrophil

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