EDITORIAL

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PATHOGENECITY & IMMUNITY IN PYODERMAS

Pathogenecity of Staphylococcus aureus (S. aureus) on human skin is well established. It is overwhelmingly the cause of primary and secondary pyodermas. Streptococcus beta haemolyticus group A is the second commonest offender in pyodermas.

Staphylococci and Staphylococcal infections:

Once the Staphylococcus enters the tissues, what factors contribute to the pathologic process? These are not well understood.

Surface antigens:

Probably there are one or more surface antigens (predominantly carbohydrates) which give antiphagocytic properties to S. aureus. These antigens are in very small amounts, but not enough to form a detectable capsule.

Exotoxins:

Alpha-toxin (alpha-haemolysin) and leukocidin have been said to be responsible for virulence of S. aureus.

The role of alpha-haemolysin in human disease is not well established, though it has been known to be injurious to human and rabbit leucocytes. It causes dermonecrosis when injected subcutaneously into rabbits.

Leucocidin destroys human leucocytes. This effect probably plays an important role in the initiation and progression of the disease. The mode of action is through leucocytic degranulation like that produced by streptolysin O and S in streptococcal disease.

Extracellular enzymes:

Presence of coagulase in staphylococcus is the generally used criteria to label the organism as pathogenic. Coagulase is probably an important factor in the pathogenecity of S. aureus. It perhaps works through three methods:

1. It promotes clot formation and thus disturbs the functioning of phagocytic cells.
2. It is responsible for deposition of fibrin on the surface of S. aureus, which acts as an antiphagocytic envelope.
3. Forms local fibrin thrombii leading to necrosis and abscess formation.

Other enzymes including hyaluronidase, lipases etc. have also been incriminated as determinants of virulence of S. aureus. These do not, however, have a major role.

Immunological response:

Most important antibodies of staphylococcal antigens are anti-haemolysin and antileucocidin. These are passively transferred through placental barrier. In fact antibodies to various staphylococcal factors are almost universally present in man since the organism is omnipresent. These antibodies are not

atleast primary determinants in resistance to infection. This is further evident from the observations that impetigo occurs despite the presence of these antibodies.

After overt staphylococcal infection, the antibacterial antibody titer rises, but the titer may not always rise when the lesions are superficial or these are treated at the very early stage. It has been observed that staphylococcal infection tends to recur even when attributed to the same microbial strain, despite the presence of antibodies. I produced staphylococcal infections of intact skin on human volunteers. The same volunteers were repeatedly challenged to the same strain of S. aureus for periods upto 6 months. I found no difference in the severity of disease process in subsequent challenges. It shows that there is no protection against staphylococcus at least in experimental conditions.

It has also been shown that immunization of experimental animals with alpha-toxins does not protect against subsequent staphylococcal disease. Instead repeated skin infections induced in rabbits result in progressively increasing inflammation. The lesions produced on the skin are more destructive than in controls. The cellular changes probably show that it represents delayed hypersensitivity reaction. It has thus been suggested that cell mediated hypersensitivity may play a role in the pathogenecity of staphylococcal infections in man particularly in recurrent infections. It has also been shown that increased susceptibility to staphylococcal infections can be passively transferred with lymphoid cells.

Streptococcus beta haemolyticus Group A :

Applying large inocula of the organism on human skin and occluding resulted in the proliferation of organisms but no manifest disease. Does this mean that it is non-pathogenic to skin? It is not true as we know now that most cases of pyodermas at least in U.S.A. are due to this organism. It thus indicates that to produce manifest lesions, streptococci need skin without its superficial layers, or it needs to be penetrated into deeper layers of skin. It is perhaps due to this reason that most of the primary pyodermas are due to staphylococci and most secondary skin infections and infected wounds and insect bites exhibit streptococci on cultural examination.

The factors responsible for the disease process with streptococcus are more clearly understood than that those due to staphylococcal infections.

Cellular components :

Both antigenic and non-antigenic components are important in human pathogenecity. Capsular hyaluronic acid is non-antigenic but is a virulence factor. It acts by impeding surface phagocytosis.

Three major classes of cell wall protein antigens are present (M, T and R). The last 2 antigens are probably not involved in virulence. M proteins inhibit phagocytosis. There are more than 50 serologically distinct M proteins on the basis of which different types of Group A streptococci are recognised. Type specific antibodies to M proteins are produced following infection and responsible for long-lasting type-specific immunity.

Group specific carbohydrate antigen of cell wall is probably not responsible for pathogenecity, and so antibodies produced to this component are not protective.

Exotoxins :

Erythrogenic toxin is responsible for the skin rash of scarlet fever. Antibodies produced during convalescence

from scarlet fever are protective against the effects of erythrogenic toxin, but it provides no protection if subsequent infection is with streptococcus of different M protein type.

Hemolysins (e.g. Streptolysin O and S) have leukotoxic properties and so play a role in pathogenecity. Streptolysin S (serum) is non-antigenic and streptolysin O (oxygen-sensitive) is antigenic.

Extracellular enzymes:

Nicotinamide adenine dinucleotidase (NADase), also called diphosphopyridine nucleotidase (DPNase) is antigenic and leukotoxic. The mode of action is different from leukotoxic action of streptolysins. It requires that cell should be phagocytosed releasing enzymes.

Streptokinase is antigenic. It activates plasmogen to plasmin. The latter is fibrinolytic. It may be the factor responsible for the spreading nature of the disease as seen in cellulitis or erysipelas.

Hyaluronidase is a spreading factor. It helps organisms to spread through tissues.

Deoxyribosenuclease (DNase) is antigenic. It hydrolyses nucleic acid and nucleoproteins released by necrotic cells such as disintegrating leukocytes. This is responsible for lack of purulence and thin character of exudate in streptococcal skin infections.

Immunological response:

Antibody response to streptolysin O and NA Dase are high after streptococcal infection of throat; whereas anti DNase and anti hyaluronidase titers are regularly increased with streptococcal skin infections.

The recurrent infections with streptococcus may be either due to different M type organisms or due to treating the disease at an early phase with antibiotics.

Anti streptolysin O offers no protection to development of cellulitis and erysipelas.

Pseudomonas aeruginosa:

This is another organism, the pathogenecity of which on intact human skin is doubted by the author. It was possible for Ps. aeruginosa to grow uninhibited under conditions of hydration for varying periods of time but no visible change other than maceration could be noticed. As it is reported that Ps. aeruginosa has keratinolytic properties, I expected that organisms after dissolving the keratin barrier would penetrate deeper, particularly when these were under occlusion, produce either local lesions or systemic effects. Maceration obtained in my studies with this organism was similar to what was obtained with other gram negative rods. It is the property of this organism to produce an alkaline reaction when inoculated on skin, which is perhaps the cause of infection. This organism cannot produce lesions on intact skin even though it can multiply on its surface.

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