The Cardio-VASCULAR System

- ○ Anatomy
- ○ Histology
- ○ Pathology
- ○ Pharmacology
- ○ Physiology
- ● Microbiology

Lec #: 1

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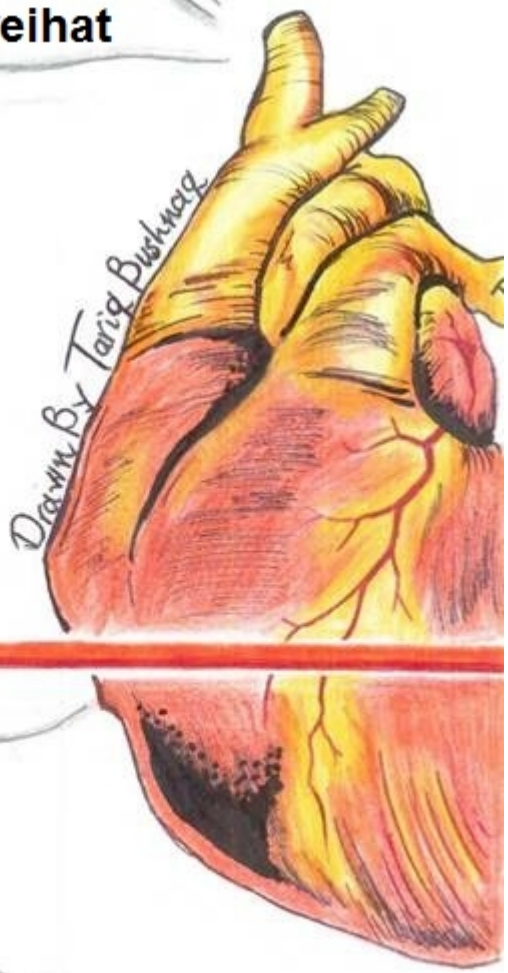
- ○ Handout
- ● Sheet
- ○ Slide



INFECTIVE ENDOCARDITIS

This topic is important especially in our country as we don't care sometimes if we have an infection in the oral cavity or from minor injuries in the skin or any part of the body. If few numbers of bacterial cells managed to enter the blood stream, they would produce **fever** of unknown origin.

Fever of unknown origin is associated with bacteremia. **Bacteremia** is not always manifested by the presence of fever or other clinical symptoms. Fever might be associated with viral infection in the respiratory tract for example.

Pathogenesis

If a bacteria persists in the blood for a short period especially in people with some abnormalities in the heart valves, post streptococcal disease, rheumatic fever...etc , it might settle on slightly damaged tissues (the heart and valves) and produce **Endocarditis Vegetation.**

Endocarditis Vegetation means the presence of **biofilm**; an accumulation of bacterial cells, platelets, fibrin and specific antibodies which together support the survival of bacteria, and this, in the long run, results in progressive damage in the tissue of the heart and might then result in **Endocarditis**.

Endocarditis is commonly manifested in people with congenital abnormality in the heart or due to previous infection with group A streptococci. So, the immune response of the body cannot penetrate the **endocarditis vegetation** (biofilm), the blood supply will not be enough, the specific antibodies cannot control the infection and the antimicrobial drugs cannot reach the infected valves. Later, we will end up with the clinical features of **Endocarditis**.

Generally, **endocarditis** in western countries is recognized in lower rates than in our region due to better medical care which protects against minor infections and reduces respiratory tract infections caused by group A streptococci. The incidence of **endocarditis** has been estimated between 3-9 cases per 100,000 patients/year in western countries. Whereas, according to a saudi study that has been done few years ago, they recorded about 100 cases/ 100,000 patients. Therefore, you always need to consider any fever of unknown origin to be

associated with **endocarditis** especially in the presence of what we call "predisposing factors".

Again, **endocarditis** is recognized more in people suffering from congenital heart disease, the presence of a previous infection, IV drug abusers, and many other predisposing factors.

Historically, rheumatic disease was one of the most predisposing factors known to develop **endocarditis** in relation to upper respiratory tract infections caused by group A streptococci. During the infection, there will be accumulation of antigenic structures and extracellular products and this will not be recognized directly as **acute endocarditis**, it will slowly develop progressive infection which will result later in **endocarditis**.

We have to distinguish between 2 major types of endocarditis:

1- **Acute endocarditis**: caused by staph aureus and viridian streptococcus, why? because usually they follow certain surgical procedures which might be associated with infection and dissemination of certain part of our flora especially in the oral cavity or skin. We can recognize two types of staph , staph aureus which produces variety of extracellular products and toxins, multiplies in the bloodstream and reach any part of the heart especially the valves if there is a previous or congenital damage.

Acute endocarditis can be recognized and be fatal within few days. If the patient isn't receiving antibiotics within the first or second week, it will be fatal or very difficult to treat. Whereas, in viridian streptococcus, the process of infection is slow and not progressive as staph aureus due to the fact that viridian streptococcus produces less extracellular products and virulent factors and it acts slowly on the cell wall antigens.

In acute endocarditis, staph aureus is more pathogenic and easily produces extracellular products which accumulate in the damaged sites and result in acute endocarditis. Whereas, viridian streptococcus is less pathogenic and associated mainly with the cell wall and there is FimA factor which is related to the cell wall and enhances the activity and pathogenicity of the organism especially during the inflammatory reaction in the heart tissue.

2- **Subacute endocarditis**: by enterococci. They are found mainly in visceral tract (GIT) not the oral cavity or the skin. Enterococcus might enter the bloodstream and produce infection. It's less important and less pathogenic but still can produce subacute **endocarditis** and is not easily

recognized. (In the slides, it's written that it is caused mainly by viridian streptococcus)

Predisposing factors for endocarditis

(acute, subacute, and rarely chronic)

1- congenital heart disorders and prosthetic heart valves. They can easily attract bacterial cells and produce biofilm (**endocarditis vegetation**).

2- Periodontal procedures which require some surgery, so large number of viridian streptococci will enter the bloodstream and produce the infection.

3- Damaged gingival tissue due to bad oral hygiene which leads to plaque accumulation in teeth. This will attract many types of microorganisms especially viridian streptococci which might later infect the gingiva (especially during brushing) and disseminate to the bloodstream reaching the heart valves.

4- Dental extractions and dental implants. In these procedures, the patient should be treated with progressive prophylactic antibiotics; otherwise he might develop bacteremia and **endocarditis**.

5- Hemodialysis which is very common because bacteria can easily disseminate to the blood through the skin and result in bacteremia.

5- Tonsillectomy.

6- Esophageal dilation.

7- Skin infections: recognized in 1% of population. Many people especially workers who are more prone to have minor lesions don't consider it very serious. These lesions can develop infections which can't be easily removed.

8- Any form of invasive techniques such as cystoscopy, colonoscopy, urethral dilation, etc. They might produce mild infection with few numbers of cells and if the immune response of the patient can't resist this mild infection, the patient will later develop **endocarditis**.

So these procedures should always be taken into consideration and the physicians should give the patients prophylactic antibiotics. (Antimicrobial prophylaxis is recommended before and after el the surgery especially in elderly patients).

Microbial Causes

Gram +ve bacteria

- In 80-90% of cases.
- Staphylococcus catalase +ve
- Streptococcus/ enterococcus: catalase -ve

(So gram stain and catalase test are important in identifying the causative agent of the disease)

A. Streptococci

This group is subdivided to: **alpha hemolytic** (viridian streptococci) and **beta hemolytic**.

Beta hemolytic is divided according to the composition of cell wall carbohydrates into many groups: group A, B, C, D (enterococcus), etc.

1. **Group A streptococcus (S. Pyogenes)** : it's the most important due to the fact that it's associated with releasing of many enzymes and toxins which contribute to the pathogenicity of this organism. Group A streptococcus has many virulence factors like **M protein** which is related to the cell wall of the bacteria**. M protein** is very important during the process of infection due to its ability to enhance the production of specific antibodies so there will be complex molecules that are associated with the presence of group A streptococci on the damaged surface. The presence of this complex structure results in autoimmunity and damage to the infected part.

Wikipedia: "M protein" is able to prevent opsonization by the alternative complement pathway by binding to fibrinogen and thus protecting the bacteria from phagocytosis.

By using of gram stain .. We can easily recognize different streptococci according to their arrangement in short and long chains or clusters and in case of enterococci they're found as diplococci or short chains.

In group A streptococci, we have treatment problems. Group A streptococci is highly susceptible to penicillin and treatment with **penicillin** or **vancomycin** will be successful only in the first stage. It's more important to prevent the post streptococcal infection and not to wait until the accumulation of extracellular products of group A in the body. So if we have throat infection especially in children, we must give **penicillin** or **vancomycin** very early as possible and to prevent the

reoccurrence of the infection especially in children. Otherwise, they might develop rheumatic heart disease which is associated with heart damage and **endocarditis**.

If the infection is caused by viridian streptococci or other groups, we have to do susceptibility tests in vitro. We have more than 10 species of viridian streptococci that might be susceptible or resistant to penicillin.

Viridian streptococci it's very common to cause all forms of **endocarditis** but mainly **subacute endocarditis** and they are commonly found in the oral cavity. In any surgical or dental procedure, we have to expect the presence of viridian streptococci that can reach the bloodstream and cause bacteremia and other complications.

In many countries, it has been found that viridian streptococcus is the causative agent of 30-40% of **endocarditis** cases. There are 2 common species; ***St. mutans*** and ***St. mitis*** which account for 90% of all cases caused by viridian streptococci. They we susceptible to penicillin but unfortunately some species became resistant. So, it's recommended to do susceptibility test to choose the proper treatment.

2. **Enterococcus** (Group D)

   is highly susceptible to **ampicillin** and **amoxicillin** and less to **penicillin** alone. We can use a combination between **penicillin** and **clindamycin** in treatment of ***enterococcus fecalis***. **Enterococcus** may become resistant; here we have to look for other antibiotics like **teicoplanin** which is more expensive ant toxic.

B. <u>Staphylococcus</u>

   coagulase +ve staph aureus.

   It's more associated in the severe forms of acute **endocarditis** and more difficult to treat because many strains are resistant to **penicillinase resistant antibiotics (oxacillin)** and considered multi drug resistant to all types of **beta lactam** antibiotics, **penicillins** and **cephalosporins**, so the only choice is to use **vancomycin**.

They are found in the skin more than the oral or nasal cavities and more associated with intravenous drug abusers or from vascular catheters that can be contaminated with skin flora of nurses and other patients which result in bacteremia and **endocarditis** .

Lab tests

1. Catalase test (staphylococci vs. streptococci)
   Catalase +ve ---> staphylococci
   Catalase -ve ---> streptococci
2. Cultured blood samples (viridian streptococci vs. beta hemolytic streptococci)
   Viridian streptococci produce partial hemolysis of RBCs in contrast to beta hemolytic streptococci that completely destruct the RBCs and this is a very useful test in differentiating between different streptococci.
3. Coagulase test (staphylococci)
   Coagulase +ve staph appears yellow or gold
   Coagulase -ve staph appears white

Due to a certain study:

1. 30-40% of the cases are caused by Viridian streptococcus
2. 5-10% by enterococcus in the intestines which is more infectious and becomes more resistant to a wide spectrum of antibiotics like cephalosporins.
3. 10-25% by other streptococci like group C and F which are rarely associated with sore throat or tonsillitis but it might produce mild infection and contaminate different surgical procedures related to tonsils and result in bacteremia.
4. Staph aureus (coagulase +ve) is more common to cause **endocarditis** than coagulase -ve staph. In some countries, staph aureus (Coagulase +ve) and staph epidermis (coagulase -ve) equally cause **endocarditis** which means that there's low hygiene standards especially in surgical procedures.

Gram -ve Bacteria

Rare.
The most common: Brucella and Salmonella typhi and paratyphi. In 1990s, there were many cases of **endocarditis** in JU Hospital are related to Brucella that produced fever but now they're uncommon.

Fungi

Candida is common in oral cavity, intestines and genital tract. So any procedure in these areas, we have to expect an infection which might develop later into **endocarditis**.

Candida, in general, rarely causes **endocarditis** but in **immunocompromised** patients and who are treated with antimicrobial drugs for a long time, we have to except an overload of candida in the oral cavity and intestines causing candidemia which might not be associated with fever which means that it's not recognized easily and then the patient develops **endocarditis**.

Other fungi that are rare include ***Histoplasma Capsulatum*** and ***Aspergillus***. these are found in severely immunocompromised patients.

We can identify candida in the lab by certain blood tests. We can notice the presence of elongations and clusters.

Treatment

is not easy to achieve but it's recommended to keep prolonged treatment with antibiotics (not less than 4 weeks) in order to be sure that the bacterial vegetation in the infected area of the heart is already removed.

Clinical diagnosis of endocarditis

Diagnosis isn't easy because not all the cases are associated with fever and Other symptoms differ between patients. So you can't rely on the clinical picture. The only ways is to do blood culture. The problem is that many physicians diagnose it using echocardiogram which might benefit only if the vegetation is large but if it's small, it can't be recognized.

Note: It's not enough to take 1 or 2 samples, why? Because the presence of the vegetation sometimes can release bacteria. At least, 3 or 4 samples (especially in immunocompromised patients) should be taken and culture for bacteria.
If +ve, susceptibility to antibiotics should be examined.
If -ve, the blood should be cultured for fungi (especially in immunocompromised patients).

Early treatment of bacteremia with antibiotics is required. If the patient doesn't respond within one week, you should do more tests.

ألا ليتَ الشّرورَ بلا نقاطٍ
وليتَ الحربَ كانت دونَ راءِ

دمتم سالمين :)

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