Infective endocarditis

Today's lecture is about infective endocarditis , the Dr started the lecture by asking what are the most common causative agents of infective endocarditis ?

1-Group A streptococci

2-Group B hemolytic streptococci

3- Enterococci

4-Staph

5- And the most important causative agent is: Viridans streptococci (part of our oral cavity flora)

infective endocarditis is always associated with fever of unknown origin especially in patients above 50 and sometimes requires a lot of investigations in order to establish why it is developed " the clinical physicians usually have more knowledge about it , here it's important to take history from the patient by asking him specific questions for example : Have you in the last few (weeks –months) got any dental procedures in relation to extraction of teeth ? Have you take any intravenous fluid ? Have you got any abscess in any part of your body ? Have you got any operation ? minor operations can be associated with bacteremia followed by infective endocarditis

Such history will help you to have differential diagnosis and to know the causative agent as a source of infection , because it is known that there are certain predisposing factors which contribute to developing of the disease

Historically , infective endocarditis has been associated with rheumatic heart disease , If the patient has (especially young patients) repetitive group A streptococci tonsillitis this might later in adulthood be associated with rheumatic heart fever as well as infective endocarditis.

Generally , this infection is related to heart valves " more than other parts of the heart " . And in this infection few numbers of bacterial cells reside at the site of injured tissue especially in relation to the congenital heart defect.

In the community there's a few percentage of those who have congenital heart disease , so bacteria reside in the site of these tissues and start slowely to release it's end products (e.g in the case of viridans streptococci it releases dextran) which is a complex of polysaccharide that attaches on the surface and begin to produce bacterial vegetations (biofilm) which cover the surface of infected tissue and it's composed of accumulation of living and died bacteria , platelets , and fibrin filaments with few numbers of leukocytes .

these bacterial vegetations work as a barrier so we can't get the advantage of the antimicrobial drugs , because it can't reach the living cells , however drugs can help depending on the size of the lesion .

The presence of infective endocarditis might be associated with several clinical features mostly congestive heart failure and might associated with some abscess.

The incidence of infective endocarditis in general healthy population has been estimated between 3-9 cases per 100,000 patient/ year in western countries , keeping in mind that the outcome can be fatal if the patient is not diagnosed or treated with antimicrobial drugs .

"In our countries there are some studies but we don't know the exact incidence ".

Now we can divide the patients into Two parts:

1- Eldery patients : whom age is between 50-60 years and now considered above 70 years old , those might develop subacute infective endocarditis not the acute type
2- Young patients especially who exposed to dental procedures , invasive technique , or drug abusers , those pts might within few days develop acute bactereima " caused by very few numbers of cells " and then develop infective endocarditis .
recently , the Most predisposing factor for infective endocarditis is congenital heart disease , then drug abusing which is very common , then Surgeries related to any part of the body and oral procedures , especially if the Dentist did not give prophylactic antimicrobial drug in certain category of patients .
In post streptococcal diseases , repeated infection in respiratory tract can be

associated with infective endocarditis but , skin infections is less associated with infective endocarditis (it's more associated with glomerulonephritis).

The Presence of prosthetic valves in the body - which is nowadays very common - will enhance the attachment of certain types of bacteria such as gram +ve bacteria - which produce dextran -"the sticky material" that helps in adhesion and this allows more and more viridians streptococci to attach to the prosthetic valves and produce the infection (prosthetic valves are responsible for 1/3 of endocarditis cases).

Generally , it's important to distinguish between acute and subacute infection . Acute type is easily recognized and often few questions will confirm the source of infection which is not necessary to be associated with certain surgical or dental procedures , the patient complains of continuous high fever , weakness... in case its associated , symptoms develops 3-5 weeks after procedures .

Whereas, the subacute type is more difficult and requires a lot of investigations in order to confirm the infection especially if the patient doesn't have rheumatic disease or prosthetic valves.

In addition , it's not easy to distinguish causitive bacteria or fungi that's found in infected patient's blood because in the subacute cases , blood has few numbers of organisms , but in acute cases you can identify it and there will be no difficulty.

Again the type of organisms that cause the disease commonly is viridians groups , to less extent streptococci and staph aureus (staph aureus is always associated with pus)

It's important to compare between the pathogenesis of organisms " the potential virulent factors produced by each one of them " : For example if we compared staph aureus with viridans , viridans are almost harmless because staph produce variant types of extracellular substances.

There are many predisposing factors for infective endocarditis , mainly congenital heart failure , prosthetic valves , pacemakers , pneumonia and

meningitis , other localized infections might later be associated with the disease.

Dental procedures are responsible for too many cases , however , bad oral hygiene - which is recognized in certain types of persons who don't take care of their oral hygiene - is also responsible for some cases , it might result in accumulation of pain and sever inflammatory reaction in gum ,other predisposing factors are dental extraction and dental implants which are very common in our country.

Hemodialysis , Tonsillectomy , Esophageal dilation or any invasive procedures , if the physician doesn't give prophylaxis for any of these factors they can be associated with infective endocarditis , specially hemodialysis which results in a difficult case .

Skin infections might be easily recognized and treated , but certain types of it is associated with minor abscess , patient might not care about it or she/he might use topical treatment like fucidin - which is misused in our country - this will mask the infection but later - after one month to one year - patient might develop endocarditis from this minor skin infection in his fingers and such cases are reported .

IV drug abusers might also develop infective endocarditis.

Other procedures are less associated like common Cystoscopy , Colonoscopy , Urethral dilation , especially in certain patients "elderly ".

The only way to help here is to give the prophylactic antimicrobial drugs , but the problem is in the dose and timing , it has been well established that the patient should be given the recommended antimicrobial drug at least 24 hours before any procedure and for at least two days after the procedure , (so in total 3 days) , some physicians give it only one day before the procedure and one day after (which is wrong) , there's a number of studies in USA established by studying thousands of cases , those studies states that patients should be given the prophylaxis for at least 3 days, but it's better to give it for 5-6 days especially in certain elderly patients who might suffer from underlying diseases .

Causative agents

Mainly, gram negative bacteria such as streptococci , then gram positive cocci which is divided into staph " staph coagulase –ve is less associated than coagulase +ve in surgical procedures related to heart and skin infection " and strepcocci which is divided into hemolytic and nonhemolytic -beta streptococci - ".

Group A streptococci is related to post streptococcal diseases which occurs due to accumulation of antigens (m-protein) of the cell wall (not the polysaccharides of the cell wall) and by this accumulation it will develop immunocomplex reaction that resulted in severe damage.

In the case of Group A Streptococci (S. pyogenes) We should isolate the organisms from patient because he started to secret the end products of theses bacteria)

we can easily recognize strep from staph under microscope but it is not enough , we should do further tests like culturing blood sample in order to recognize beta hemolytic that causes complete destruction of red blood cells and later we identify it by certain biochemical test by using specific antiserum for group A "remember that group B are more associated with vagina and neonatal sepsis and meningitis , it is not related to infective endocarditis " , the other groups like C ,G,F rarely cause the disease but it might be associated directly like viridans not like group A by post streptococci disease.

for staph at least we should know if it is coagulase +ve or –ve , in Staph aureus the colony is golden in color and it's coagulase +ve , these two tests with catalase is enough .

Viridans streptococci

responsible for 30-40 % of infective endocarditis cases , it's always associated with secretion of dextrans which is a complex originates from fragmentation of polysaccharide and it is a sticky material that allows the organisms to adhere to the surface of injured heart valve , and by the Fibronectin-binding protein reaction which attracts platelets and produces vegetation "More important in dental procedures and gingivitis " .

The doctor explained the table in the slides which is obtained from American references by collecting more than 2000 cases of infective endocaritis over 5 years:

for Enterococci species it is responsible for 5-10% of cases , it is few percentage but the case is more complicated and fatal , if we compare it's pathogenesis with viridans , enterococci is more virulent than viridans , Because enterococci is more resistant to many types of antibiotics (all cyclosporines can't be used as a result for its cell wall, also beta lactam can't be used and Aminoglycosides can't penetrate the cell membrane , vancomycin can be used but it is not so effective alone because enterococci can develop resistance against it so fast)

The treatment will be by combination of two antibiotics Aminoglycosides and a type of beta lactam drug "ampicillin or amoxicillin" , in relation to subacute endocarditis it's not easy to isolate the organism or to know or even to guess the causative agent and how we treat it (the organism is isolated in less than 10% of cases) so , it requires experiment and the patient might die during treatment because sometimes if the first drug was not effective, by the second drug the disease develops to cause more damage and leads to death .

But other streptococci don't have problem with antibiotics because it responds to pencillin , ampicillin , amoxicillin and less resistant even to either microlide or vancomycin so they are very effective against it .

For staph aureus it's important to know if it MRSA or not (MRSA +ve or –ve) if it was resistant we should select vancomycin .

For coagulase –ve there's a problem despite the fact that it is less pathogenic but can be resistant to different types of antibiotics.

You should relay on the antimicrobial resistance test.

Gram-negative bacilli rarely is associated with the disease " the doctor only remembers one case of salmonella that causes infective endocarditis and it was very difficult case " , but Brucella is associated with more cases and the treatment is difficult and complicated.

Fungi as a causative agent affect immunocompromised patients but it can also affect normal people but to a much lesser extent.

Finally, there are certain cases due to other organisms , in these few cases we require sophisticated technique following the death of pts in order to recognize the causative agent .

For yeast you should know if the patient had crush in the oral cavity or in any part of his body , so he has Candida . In addition if there's signs or symptoms that indicate a problem in the heart so this will be due to candida especially if patient is immunodeficient .in this case diagnosis is'nt easy .

In case of respiratory intubation and catheters which might later produce injures during insertion of tube followed by infections with candida that produce biofilm and can reach the subcutaneous tissue and form fatal localized infection or endocarditis .

In case of Aspergillus , it is very rare and not recognized often in our hospitals

For Histoplasma capsulatum it is related to USA and very rare and we can confirm the infection following death of patient .

What can help you to recognize Candida albicans ? It's filaments and culturing it isn't difficult .

Lastly, diagnosis and treatment

There's clinical diagnosis (which we will learn in the hospital) especially cardiogram and ultrasound to recognizes the presence of lesions and we have clinical signs and symptoms for acute and subacute infections .

In relation to laboratory it is well known that in infective endocarditis (the acute type) it is easy to discover the organisms " for about 50% cases and above we can recognize the organisms which are mainly viridans then staph , but in the subacute type there will be a problem because the physician should send at least 3-5 blood samples within a week especially if symptoms are associated with elevated body temperature , but unfortunately many of our pts they don't like always to give blood , they think they lose their energy , so it's not easy to take blood samples(5 ml of blood) from pt within one week especially elderly people.

What happens clinically that the attending physician will not take 5 ml of blood which is the minimal amount in order to recognize organisms in blood stream , he takes only 1 or 2 ml and this always gives a –ve result so dr prefers to take blood two times for each time 4 samples with 1-2ml .

So the amount of blood Is important in order to recognize bacteremia or septicemia "in case of septicemia 1ml of blood can discover it easily but this is not true for bacteremia."

Then doing the proper antimicrobial test , these require a lot of experiment that a lot of physicians lack.

In our country and in our hospital the majority of staph aureus , up to 90% considered resistant to beta-lactam drugs (metacillin resistant) , so we can use vancomycin but it's an expensive drug .