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Review Article

Infective Endocarditis Resulting in Septic Cerebral Infarction

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- 66 years old male IW admitted to A&E for 2/52 Hx of lethargy and generally unwell. Mild drossiness and reduced oral intake and mobility.
- Initial blood results showed Leucocytosis (WBC=22,000, CRP=97, NEU= (20.18), and PCT= 1.07), furthermore, AKI on CKD secondary to dehydration(Urea= 26.7).
- Initial diagnosis was sepsis, and Vasculitis-IgA=4.71,ANCA=negative, Complements= normal (Blood Cx were taken 3 sets as per micro, and Vancomycin was initiated), with Positive Flu A
- ABG showed mild hypocapnia.
- U/A Proteinuria.

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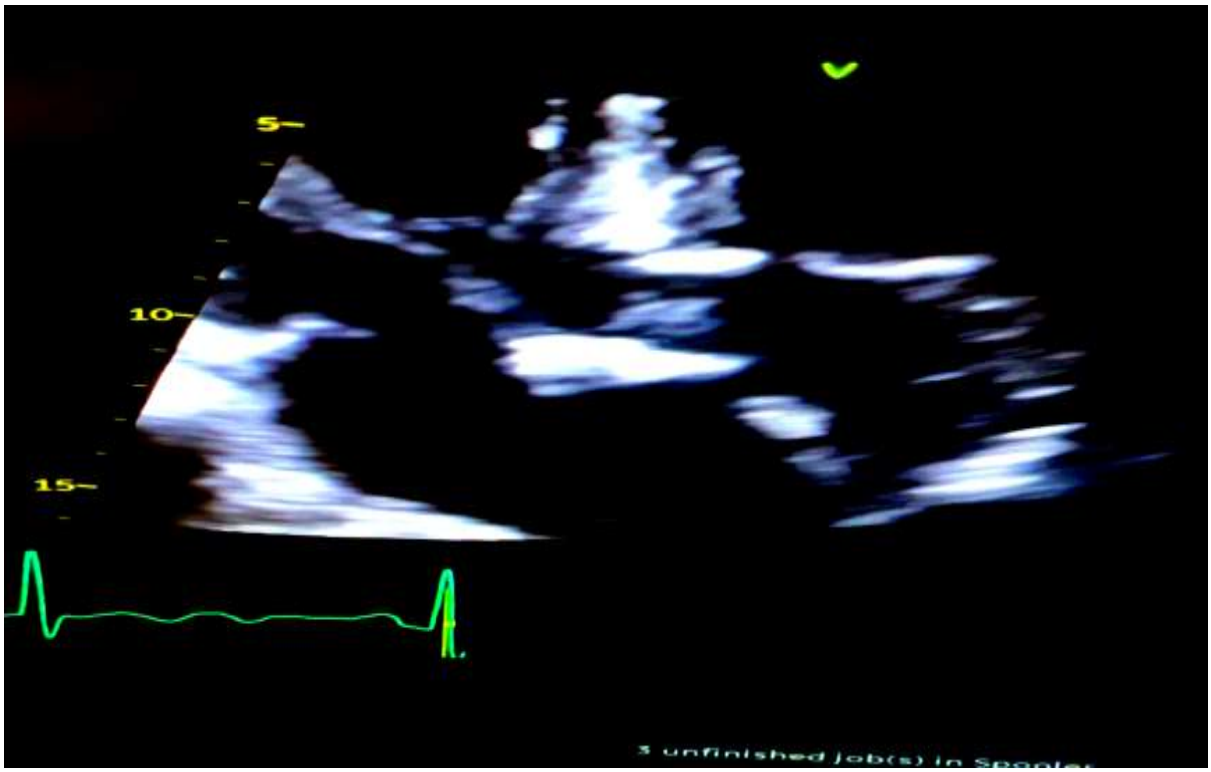
- ABG showed mild hypocapnia.
- U/A Proteinuria.
- PMH: SAH(coiling 3years ago)
    - AVR 2018
    - TIA 10 years ago
    - Dyslipidemia
    - OA
    - Rt.Adrenal adenoma
    - Lung Granolomatosis
- Physical examination: GCS=12/15, Mild drowsiness, Power 4/5 upper and lower extremeties, no Nystagmus. Vital signs= acceptable, Afebrile.
- CVS= No CP, No SOB , Blowing diastolic murmur, prominent at left sternal edge, equal pulses, no carotid bruits, no murmur radiation. Normotensive, HR=70-75 , Rt. hand palmar erythema, and mild splinter haemorrhage. Upper and Lower extremities pulses equal, with no delays. EKG= no RVH strain, LVH, no signs of STEMI or NSTEMI (although trop was= 250, most probably high trop due to sepsis)
- Abdomen= soft, no bowel habit changes
- LL= No swelling, preserved peripheral pulses.
- Resp= GBAE, no crackles or any end-expiratory wheezes.

- MRI= Imaging shows extensive abnormality of mixed age. There is background multifocal haemorrhage which would suggest an angiopathy however there are areas of more acute abnormality with apparent acute/subacute infarcts identified on the diffusion weighting.

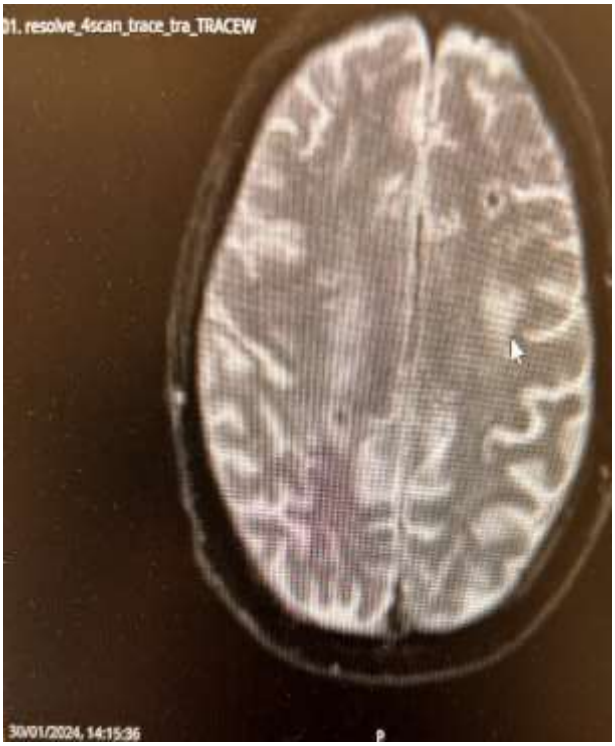
CT Intracranial Angio:

He has known previous aneurysm with coiling He presented with lethargy over 10-days. No report of sudden onset headache He has a few small patches of SAH but no blood in basal cisterns. This can happen with delayed presentation due to redistribution of blood. He has a cerebellar infarct CTA in first instance to look for recurrence or new aneurysm Also needs MRI as per your radiologist to look for vasculitis.

Echocardiogram:



MRI Image:



QUICK Reflection:

- General lethargy for two weeks.
- Decreased mobility.
- History of AVR.
- Diastolic murmur , with mild dermatological manifestation.
- Positive Blood cultures (Staphylococcus Epidermidis) 2: Staphylococcus epidermidis ranks as one of the most common species to cause infective endocarditis in both the prosthetic valve and the native valve. Up to 40% of cases of prosthetic valve endocarditis (PVE) are due to coagulase-negative staph.
- HIGH risk of Endocarditis , with positive echo of AV vegetation. 2

- Positive MRI for Ischaemia.
- Splinter haemorrhage. 1

Primary Diagnosis : IE

Definition:

A condition in which the tissues lining the inside (the endocardium) of the heart and the heart valves become inflamed (red and swollen). Endocarditis was first described by William Osler in 1885. Developments in medical science and research in microbiology have contributed to a better understanding of the disease. The most common risk factors for infective endocarditis are previous heart damage, recent heart surgery or poor dental hygiene.

No race or ethnicity is more affected than others. Prognosis of infective endocarditis remains poor despite advances in diagnosis and therapies. Mortality rates are approximately 25% even with the best therapies available. Female sex is less common in patients diagnosed with IE (unknown reason), but mortality is higher.

Risk factors :

- Although the heart is usually well protected against infection, it may be easier for bacteria to bypass the immune system in people who have:
- An artificial (prosthetic) heart valve
- Valve replacement surgery congenital heart disease – where a person is born with heart defects
- Hypertrophic cardiomyopathy – where the heart muscle cells have enlarged and the walls of the heart chambers thicken
- Risk factors that contribute to the onset of Infective Endocarditis include:

- Intravenous drug use with a needle contaminated with bacteria or fungi
- Presence of an artificial (prosthetic) heart valve or other valve repair material
- Presence of a cardiac pacemaker lead
- Previous infective endocarditis
- Mitral valve prolapse with valve leakage
- An aortic valve with only 2 (instead of the normal 3 valve leaflets). This condition, called a bicuspid aortic valve, is present in about 1% of people.
- Narrowing (stenosis) of the aortic valve due to age-related calcification
- Other abnormal valves caused by rheumatic fever and degenerative conditions
- Congenital heart disease, especially if repaired with artificial material.

Endocarditis can be broken down into the following categories :

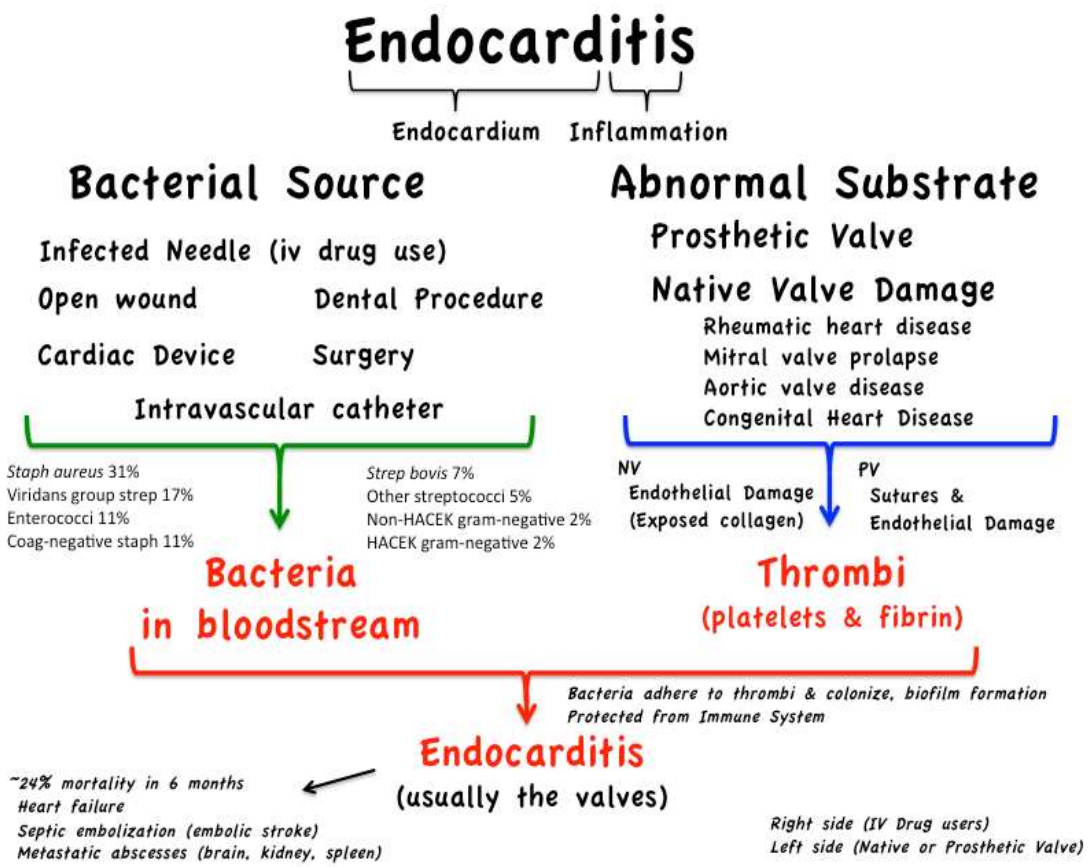
Native valve endocarditis (NVE), acute and subacute: gram-positive bacteria such as Staphylococcus aureus, viridans group streptococci, Streptococcus bovis, and enterococci (Gould et al, 1975; Chambers & Bayer, 2020).

- Prosthetic valve endocarditis (PVE), early and late: Prosthetic valve endocarditis (PVE) can occur early or late after surgery, and the bacteria causing early vs late infections tends to differ (Karchmer, 2017). Early infections (S aureus and S epidermidis) are caused by bacteria that are able to stick to surfaces that are not endothelialized (e.g. sutures, valve sewing ring), but have become coated with host proteins such as fibronectin and fibrinogen. Late infections (streptococci) are more commonly caused by bacteria that adhere to tissues that have become endothelialized after several months following valve replacement. These pathogens more closely resemble those causing native valve endocarditis (Karchmer, 2017).

- Intravenous drug abuse (IVDA) endocarditis, (right side of the heart) : S. aureus is the most common cause of IDU-IE (accounting for more than half of all cases). Streptococci and enterococci are the next most common pathogens (Sexton & Chu, 2017).

- Acute infective endocarditis develops suddenly and may become life threatening within days. Subacute infective endocarditis (also called subacute bacterial endocarditis) develops gradually and subtly over a period of weeks to several months but also can be life threatening.

- The tricuspid valve is most commonly affected (50%), whereas involvement of the mitral and aortic valves is less common (20% each).



Organisms in IE :

IE has a large number of causative organisms :

- Streptococci. These account for 50%–80% of IE cases. ...
- Staphylococci. Staphylococcus aureus and Staphylococcus epidermidis account for 20%–30% of subacute cases of IE and 50% of the acute forms. ...
- Enterococci. Enterococci account for 5%–15% of IE cases. ...
- HACEK (Haemophilus species, Aggregatibacter actinomycetemcomitans, Cardiobacterium hominis, Eikenella corrodens, Kingella kingae) organisms. Negative blood Cx
- Marantic endocarditis is characterized by the presence of sterile vegetations in the heart valves, and is associated with hypercoagulability states (cancer, autoimmune diseases, HIV). Its main complications are stroke, pulmonary thromboembolism, acute intestinal ischemia and splenic, renal and hepatic infarcts. Marantic endocarditis, Libman-Sacks endocarditis, NBTE, typically associated with cancer and collagen vascular diseases: should be considered in patients with culture-negative endocarditis and elevated inflammatory markers.

Criteria for the Dx of Endocarditis:

Table 34.2. The Modified Duke Criteria Definitions of Definite, Possible, and Rejected Endocarditis

Definite IE

- Pathologic criteria
  1. Microorganisms demonstrated by culture or histologic examination of a vegetation, a vegetation that has embolized, or an intracardiac abscess specimen; or
  2. Pathologic lesions; vegetation or intracardiac abscess confirmed by histologic examination showing active endocarditis
- Clinical criteria (see Table 34.3)
  1. Two major criteria
  2. One major criterion and three minor criteria
  3. Five minor criteria

Possible IE (see Table 34.3)

1. One major criterion and one minor criterion
2. Three minor criteria

Rejected

1. Firm alternate diagnosis explaining evidence of IE
2. Resolution of infection endocarditis syndrome with antibiotic therapy for ≤4 days
3. No pathologic evidence of IE at surgery or autopsy, with antibiotic therapy for ≤4 days
4. Does not meet criteria for possible IE, as described previously

IE, Infective endocarditis.

Modified from Li, J. S., Sexton, D. J., Mick, N., Nettles, R., Fowler, V. G., Ryan, T., et al. (2000). Proposed modifications to the Duke criteria for the diagnosis of infective endocarditis. Clinical Infectious Diseases, 30(4), 633–638.

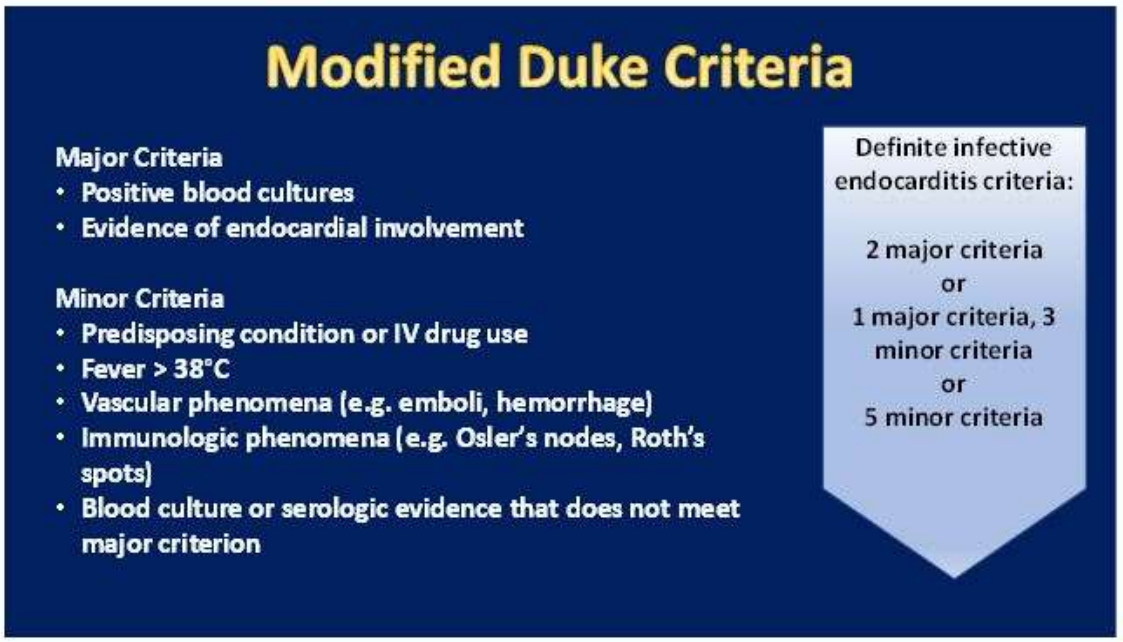


Figure 2: Modified Duke Criteria for the diagnosis of infective endocarditis [2]

ESC criteria for IE:

TABLE 2. European Society of Cardiology 2015 Modified Criteria for Diagnosis of Infective Endocarditis[2]

Major Criteria	Minor Criteria
• Persistently positive blood cultures from 2 seperate culture sets • Echocardiogram: vegetation, dehiscense of prosthetic valve, asbcess, valvular perforation, or aneurysm • Abnormal findings around the prosthetic valve 18F-FDG PET/CT (if the prosthesis was implanted for >3 months) or radiolabelled leukocytes SPECT/CT • Cardiac CT demonstrating paravalvular lesions	• Predisposing cardiac condition or IV drug use • Fever >38.0 °C • Vascular: emboli, hemorrhages, Janeway lesions, aneurysms, • Immunlogic: glomerulonephritis, Osler nodes, Roth spots, rheumatoid factor • Positve blood cultures not meeting major criteria

CT, computed tomography; **PET**, positron emission tomography; **SPECT**, single photon emission computerized tomography

Manifestation of IE:

- Vascular phenomena Arterial embolism- sudden interruption of blood flow to organ or body part due to clot (embolus)
- Septic pulmonary emboli-blood clots in the lungs containing bacteria
- Mycotic aneurysm- dilation of an artery due to infection damaging vessel wall
- Intracranial haemorrhage- brain bleed
- Conjunctival haemorrhages- rupture of blood vessels in the eye
- Janeway's lesions-nodules on palms of hands and soles
- Right-sided lesions typically produce septic pulmonary emboli, which may result in pulmonary infarction, pneumonia, or empyema. Left-sided lesions may embolize to any tissue, particularly the kidneys, spleen, and central nervous system. Mycotic aneurysms can form in any major

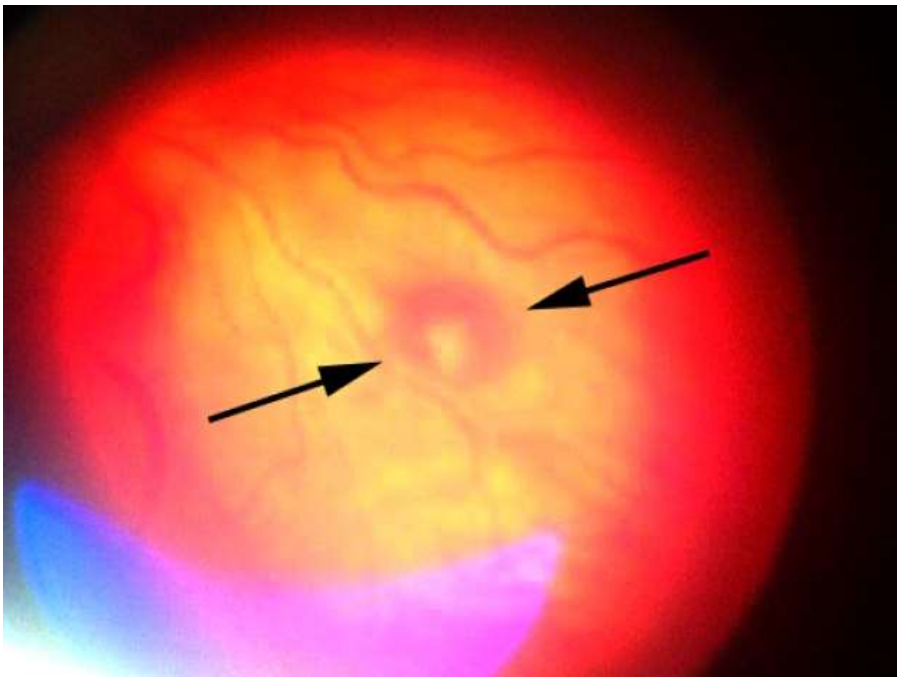
artery.

- Endocarditis is indicated by: Osler's nodes – tender lesions found on finger pulps and thenar/hypothenar eminences Janeway lesions – transient, nontender macular papules on palms or soles. splinter haemorrhages.

- Acute ischemic stroke is the most common neurological complication of IE, manifesting clinically in 20% to 40% of patients with IE.

- Septic emboli are a common complication of infective endocarditis. Septic emboli could affect multiple organs and cause variable insults. Blood cultures are usually positive in patients with septic emboli. Septic emboli cause tissue injury by two different mechanisms: ischemia and infection. The vegetations itself and the bacterial toxins that are produced can cause irreversible valvular damage, which manifests as valve insufficiency or regurgitation on echocardiograms. In the acute phase of IE, vegetation particles enter the blood circulation, causing vascular embolism and local vascular inflammation.

Roth Spot



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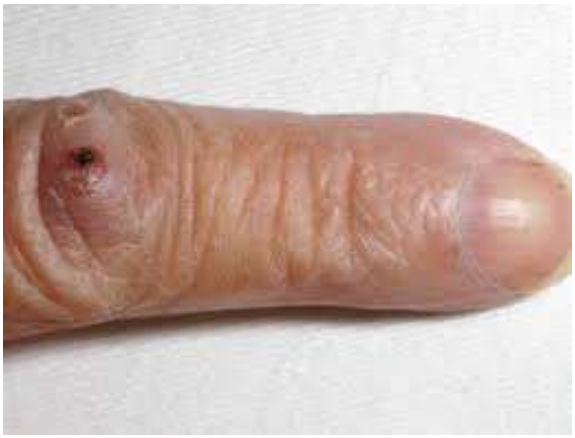
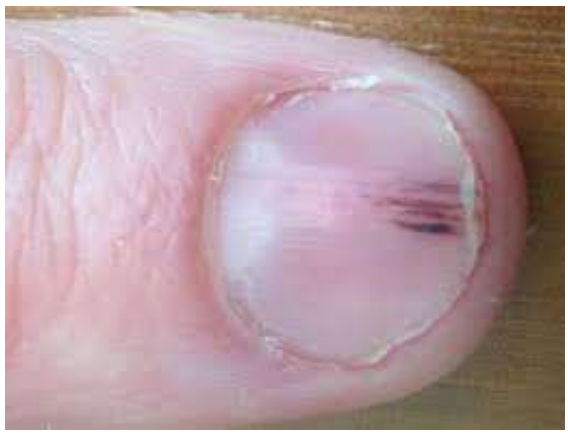
Osler Node/ Janeway lesion



Splinter haemorrhage



Dermnet

Septic Emboli due to IE:

- Infective endocarditis is an established common cause of septic emboli from case studies as early as 1883. Parts of the vegetations on the valves infected dislodge and travel through the bloodstream and block blood vessels based on the size and the location. Previously, septic embolism was almost exclusively a complication of septic pelvic thrombophlebitis secondary to both septic abortion and post-puerperal uterine infection. Currently, risk factors for septic emboli include intravenous drug use, indwelling vascular catheters, and patients with prosthetic cardiovascular devices.

- The rate of septic emboli among patients with infective endocarditis varies widely among studies. In a study including 437 patients with surgical endocarditis, septic emboli were present in 10.52% of patients with infective endocarditis. Also, systemic embolization complicates about 20% to 50% of cases of infective endocarditis of left-sided heart valves. Another study, including 493 with Infective endocarditis, septic embolism was diagnosed in 57% of cases of infective endocarditis. In a systematic review and metanalysis, the pooled prevalence of septic embolism in patients with infective endocarditis accounted for 25 %. Septic embolization occurs in at least 30% of patients with infective endocarditis referred for cardiac valve replacement.

- Right-sided endocarditis vegetations usually embolize to the lungs and cause septic pulmonary emboli. Patent foramen ovale (PFO) is a congenital cardiac anomaly that correlates with cryptogenic strokes and may provide a conduit for paradoxical emboli. Left-sided endocarditis vegetations usually embolize to the brain, causing strokes (occlusion of cerebral arteries by emboli derived from endocardial vegetation)

Types of Septic Emboli:

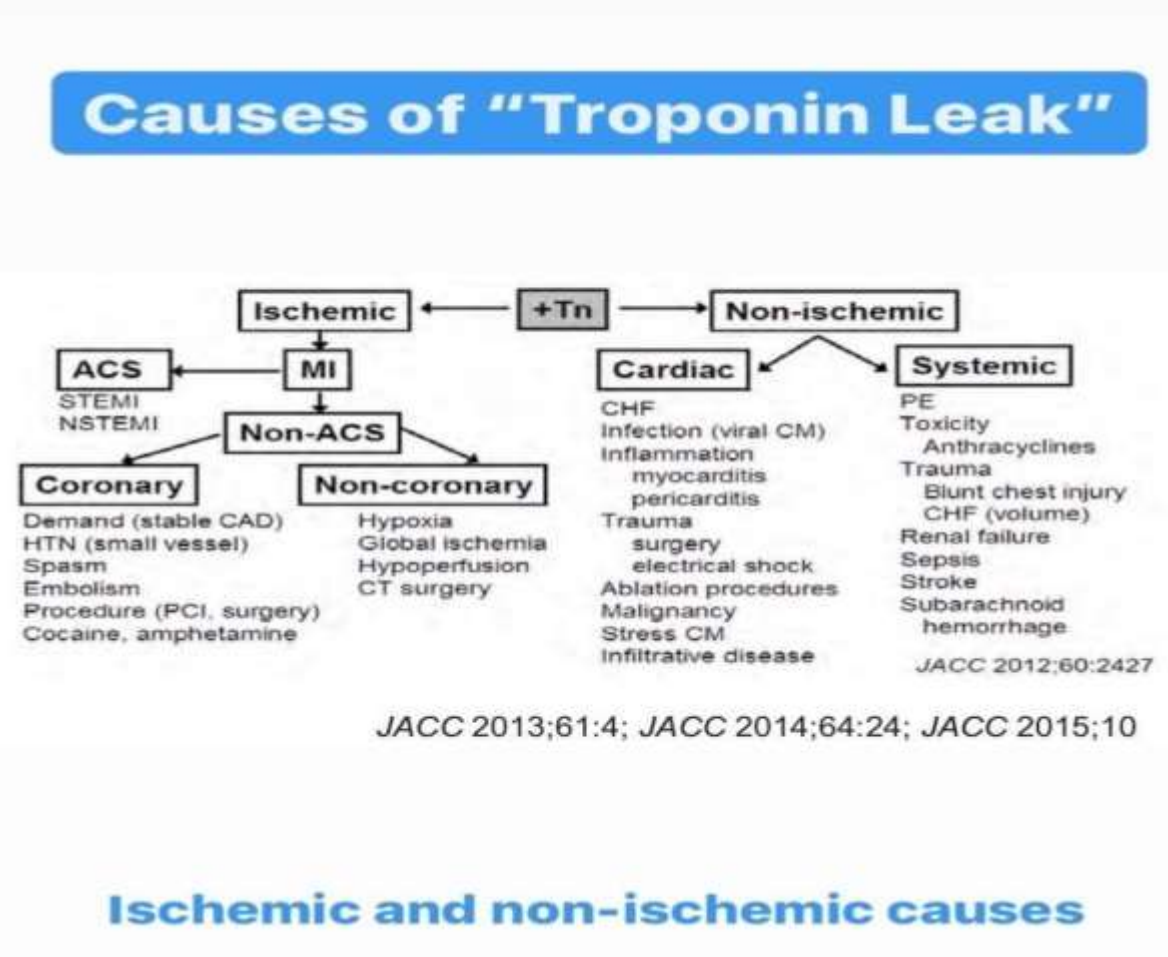
- Septic cerebral emboli
- Septic splenic emboli
- Septic coronary artery embolization
- Septic mesenteric emboli
- Pylephlebitis
- Pyogenic liver abscesses
- Septic emboli of the extremities
- Septic emboli of the skin (Janeway lesion of bacterial endocarditis)
- Lemierre syndrome (is an acute oropharyngeal infection caused by Fusobacterium necrophorum with secondary septic thrombophlebitis of the internal jugular vein (IVJ)
- Septic retinal emboli
- Symptoms and signs of neurological deficits depending on the stroke location and the extent of infarcted/inflamed area, and the number of the affected areas. Embolism to the brain in a patient with infective endocarditis can be clinically silent. In one prospective study of 56 patients with left-sided endocarditis, embolization to the brain was detected on MRI scan in 80% of cases and

was subclinical in 48%.

- Septic emboli could affect multiple organs, and complications depend on the organ affected and the size of the embolus.

- Septic cerebral emboli could result in ischemic strokes due to infarction of the ischemic area, brain abscesses causing variable neurological deficits based on the location affected, and the extent of the damage. Septic cerebral emboli are also a risk factor for thrombolysis-related hemorrhagic transformation.[44] Intracranial mycotic aneurysms are relatively rare, accounting for less than 10% of neurologic complications of infective endocarditis.

Good to know about trop raise:



"Patient Consent was Taken"

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