

CNS

Microbiology



Sheet



Slide

Number

3

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Introduction:

First two lectures we talked about acute and chronic meningitis, which is considered an emergency situation. If you remember, CSF examination in meningitis was quite important. However, CSF examination in infections of today's lecture is not recommended.

This sheet is talking about a group of diseases which are suppurative (pus forming). Also, they occupy space in the brain. So, again, these diseases are suppurative, space occupying lesions within the brain.

Keep in mind that symptoms of brain infections are quite similar. For example, fever and headache, which are symptoms of meningitis, could be seen also in suppurative diseases and almost all infections in the brain. But in the presence of meningeal signs like neck stiffness, positive Kernig's and Brudzinski's signs, we should suspect meningitis.

(Kernig's and Brudzinski's signs can be -ve and still the patient have meningitis)

let's start taking about these suppurative space occupying diseases. The first one is brain Abscess.

1) Brain Abscess

Definition:

a brain abscess is a focal (confined to a certain space), suppurative (pus forming) infection within the brain parenchyma, typically surrounded by a capsule. The term **cerebritis** is often employed to describe a condition that precedes abscess formation when the infection is not walled off (non encapsulated).

Symptoms of brain abscess include Fever, headache and some focal neurological signs depending on where the abscess is found.

Etiology:

Similar to meningitis, brain abscess may develop due to the pathogens reaching the brain parenchyma through:

1) hematogenous spread of a septic embolus (embolus filled with bacteria), this embolus could seed somewhere within the brain.

2) after neurosurgical procedure.

For example, following craniotomy there could be seeding of certain bacteria like Staph aureus.

3) By direct spread from a contiguous longstanding cranial site of infection such as sinusitis, otitis media, mastoiditis, or dental infection.

Note: we could see around the abscess some edema

Epidemiology:

In general, brain abscess is rare , especially if you are immunocompetent.

Predisposing conditions include: long standing otitis media, sinusitis and dental infections. Also, immunocompromised hosts with underlying HIV infection, chemotherapy, organ transplantation have higher risk to develop brain abscesses

Pathophysiology:

the process starts with invading bacteria that are going to the brain tissue. Immune resident cells and some specialized non immune cells sense the presence of the bacteria and start secreting the inflammatory mediators which first recruit neutrophils. Neutrophils come and try to kill the bacteria but at the same time they could damage the surrounding tissue. And then when the process continue, more neutrophils are recruited and they die. So at the end of the process, there are dead and life bacteria .Also, there are dead and life WBC's. All of these cells will be surrounded by a fibrous capsule. And that's what we called abscess. So in abscess you suspect to see cells debris of WBC's and bacteria, and maybe you see also extracellular DNA.

Understanding the process of how abscess is formed and how it's enclosed by a fibrous capsule is important, because it has implication on treatment. For example, when we give antibiotics, which have low penetrance through the capsule, we expect that antibiotics will not be able to reach into the abscess and treat the condition. Antibiotics have low penetrance through the capsule because the blood vessels which carry the drugs are outside the capsule and can't go through it.

But if the antibiotics are not working, so what we do? We try to drain the abscess and then we give antibiotics.

Causative microorganisms:

A) In Immunocompetent patients :

In this case, Causative microorganisms mostly depend on the primary focus of infection.

1) The primary focus of infection is ear, sinus, or mastoid bone.

In this case, the most common organisms of these infections are streptococcus and most commonly streptococcus pneumonia, H.influenzae , enterobacteriaceae and bacteroids.

****keep in mind** that most famous bacteria of enterbacteriaceae is E.coli which is found in the GUT and a common cause of UTI.

****Keep in mind** that Bacteroids are anaerobic bacteria which are found normally as GUT flora.

2) The primary focus of infection is endocarditis.
in this case , the causative organism is Staph aureus or Streptococcus .

3) In neurosurgery

In this case, you expect Staph aureus and Staph epidermidis and that's because they are found on the skin.

B) In Immunocompromised patients

In this case, we start looking at one of the opportunistic pathogens like Toxoplasma gondii, Listeria monocytogenes, Norcardia and fungal infections. Keep in mind that if you see one of these pathogens you should suspect immunocompromised patient.

Clinical presentation:

1) General symptoms like headache and fever.

As we talked previously in the lecture, symptoms of infections in the CNS are very similar to each other (headache and fever). However, in case of brain abscess there is no meningeal signs, because the meninges are not affected, the infection is only in the brain parenchyma.

2) Signs of increased intracranial pressure, especially if the abscess is big.

3) Focal neurological signs

Depending on where the abscess is formed, we have symptoms, for example if the abscess is in the right frontal lobe, we expect left hemiparesis (weakness in the contralateral side) or hemiplegia (paralysis in the contralateral side).

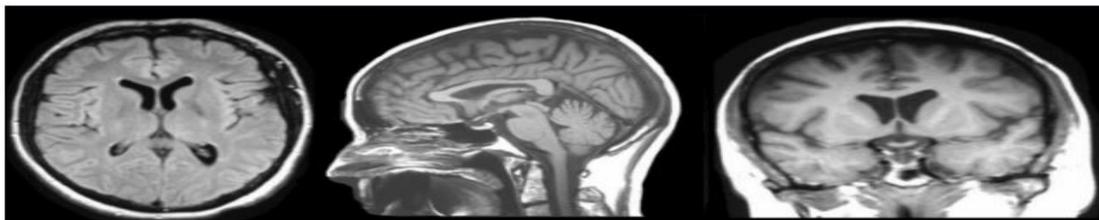
Diagnosis:

In cases of space occupying lesions we said we won't do CSF analysis because it's not useful for diagnosis. Also, CSF analysis is contraindicated in case of increased intracranial pressure, because of the risk of herniation.

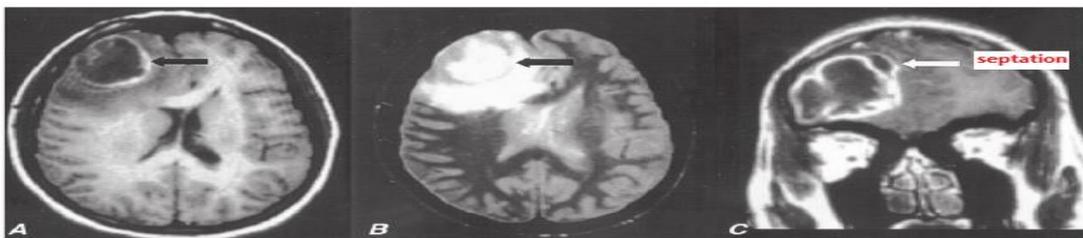
What help us in diagnosis are brain imaging techniques like MRI and CT scan. Although MRI mostly is superior to CT scan, there is place for both.

*The doctor said he doesn't expect us to recognize imaging techniques now and know the pathology, but we have to have an idea about how lesions look like.

So here we have a normal brain MRI, and if we compare it with the lower brain MRI, we can see big lesions there, and this is a brain abscess. Also, within the brain abscess itself sometimes we could have septations where the brain abscess forms like small rooms.



Normal brain MRI



Other than brain imaging, blood culture could be helpful because as we said, sometimes abscess is related to **hematogenous spread**. So the pathogens could still be found in the blood.

Treatment:

As any abscess, we should start with drainage + antibiotics. Also, we should give empirical antibiotics like 3rd generation cephalosporin to cover most gram +ve bacteria like *Streptococcus pneumoniae* and so on. Also, you can add vancomycin if you suspect *Staph aureus*.

**keep in mind that we start empirical therapy but later on we need culture to know what the pathogen is, and then we give the proper antibiotics.

Q: how do we follow up the patient after drainage of brain abscess?

We do brain imaging to make sure that the abscess isn't recurring.

Prognosis:

Now with the enhanced neuroimaging techniques like CT scan and MRI and improved neurosurgical treatment there is decreased mortality from brain abscess, but we still always expect some consequences of seizures, weakness and aphasia.

If you remember in meningitis, we expect hearing loss. Or in children, we expect developmental retardation.

the second lesion we are going to talk about is subdural empyema or pus formation within the subdural space (between dura matter and arachnoid matter).

2) Subdural empyema

-This infection is rare, it accounts for 15%-20% of all focal suppurative CNS infections, and there is predilection for young males because the infection that happens in the subdural space usually comes from infected sinuses, and because of the difference in development of sinuses between males and females it was found that the incidence in males is much higher than in females. Keep in mind that subdural empyema is related to chronic infection of the sinuses.

-Symptoms of subdural empyema are similar to other CNS infections like fever, headache, focal neurological signs, and maybe increased intracranial pressure.

-One thing that stands out in subdural empyema is that it can **deteriorate rapidly because the space isn't walled off**, the space between the dura and arachnoid is open, so as the pus forms it starts to go around everywhere where the space is between the dura and arachnoid matter.

-The causative pathogens in subdural empyema are quite similar to brain abscess, because both come from sinuses. So, pathogens that cause chronic sinusitis are expected to be the causative agents of subdural empyema, like Streptococcus, Staphylococcus, Enterobacteriaceae like E.coli and Klebsiella for example, and anaerobic bacteria like Bacteroids.

But we also have other types of empyema that can happen not from sinuses, instead, they directly come from brain trauma and skull fracture and so on, in these cases we suspect Staphylococcus.

-As we said in brain abscess, in empyema also we can find contralateral hemiparesis or hemiplegia depending on where the empyema is taking place.

Diagnosis:

Again we need to do brain imaging, CSF analysis will not help and should be avoided.

Note on the MRI here, that the subdural space is filled with pus.

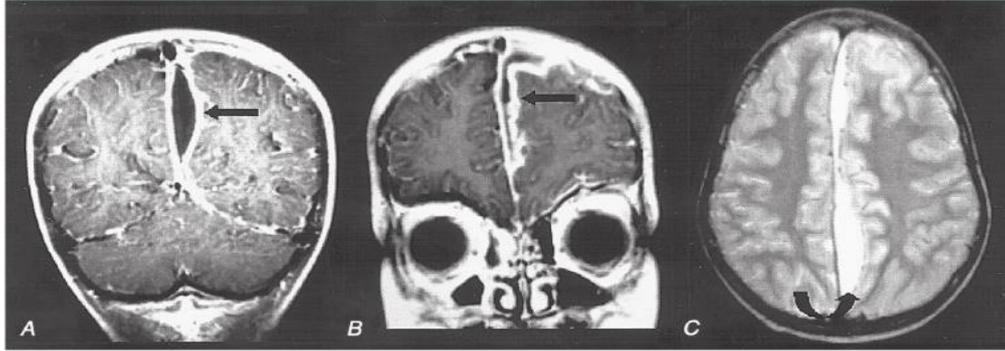


FIGURE 36-6

Subdural empyema. There is marked enhancement of the dura and leptomeninges (A, B, straight arrows) along the left medial hemisphere. The pus is hypointense on T1-weighted

images (A, B) but markedly hyperintense on the proton density-weighted (C, curved arrow) image. (Courtesy of Joseph Iurito, MD; with permission.)

Treatment:

Again we need to drain the empyema most of the time, so we need to take part of skull out in what we call craniotomy or craniectomy.

Q: What is the difference between craniotomy and craniectomy?

In craniotomy we take out the bone and then put plates and some screws, but in craniectomy, we remove the bone and then retain the same bones.

we drain the empyema by just making a small hole and through it we can do the drainage (burr hole drainage), or you can connect the holes to take out part of the skull. Also, you have to give empirical antibiotic therapy with 3rd generation cephalosporin to cover gram positive, vancomycin for Staph aureus, and metronidazole for Bacteroids.

But after giving empirical treatment, we need to do culture media from the pus, and so we know what the organism is and start giving specific therapy.

Something that is similar to subdural empyema, we have what we call epidural abscess.

3) Epidural abscess

-This infection is not between the dura and arachnoid, this one is between the dura and the skull, and that's why it's found in the form of abscess, because the dura matter is closely adherent to the skull so any pus formation will be walled off because of the strict adherence of the two layers, so pus will accumulate in the form of abscess. On the other hand, in the case of subdural empyema, the dura matter and arachnoid matter are not adherent, it's an open space and the pus will keep forming between the two layers, so we call it empyema.

- In the case of epidural abscess, you will not expect hematogenous spread, in this case the infection mostly seeds either directly after cranial surgery or trauma, or from nearby bones like sinusitis, otitis media and so on.

-The presentation, diagnosis, the causative organisms and the empirical treatment we will use are very similar to subdural empyema.

-If you compare subdural empyema and epidural abscess we expect the epidural spread to be slower because as we said the skull and the dura are adherent. (Focal neurological deficits due to epidural abscess are uncommon due to the small size of the lesion)

Finally, we have a condition that accompanies other CNS infections like meningitis, abscesses and subdural empyema but how it accompany all of those?

4) thrombophlebitis

it's something that happens within the veins.

But How?

The veins that drain sites of infection can also be infected and damaged ,and with the damage that takes place in the veins , a thrombus can form ,and this will prevent blood flow through out these veins. That's why this condition is called "thrombophlebitis".

-Also, phlebitis could occur, and phlebitis means inflammation in the veins. Keep in mind that this inflammation is suppurative because it is related to pus formation.

-Again, this condition is a complication of other infections like meningitis, epidural abscess and subdural empyema.

-what happens in thrombophlebitis is, sometimes the clot might form in any site after an infection, and then, it can drain into another sinus within the brain and spread. So finally if the patient died and you look at the brain you can find many places of thrombosis , the veins are damaged and the pus are moving around and so we have suppurative thrombophlebitis .

Q: How can you know for sure that the patient has thrombophlebitis?

if you expect that blood flow is hindered within the blood vessels ,you do some imaging that can show you the blood flow in these blood vessels and also you can see narrowing in the vessels where thrombosis is taking place .

Treatment:

First of all, you have to treat the underlying infection by giving antibiotics and try to take out the thrombus that closes the vein.

-Some people give anticoagulants so the thrombus can dissolve.

SUMMARY

So finally the infections we have covered starting from the outside: epidural abscess which commonly comes from direct spread either from infected bones or from the outside.

Then we have subdural empyema, we said that this one spread faster because it's in opened space between the dura and arachnoid matter. Also, it's commonly associated with chronic sinusitis. Then in the subarachnoid space we have meningitis .And then meningitis can be accompanied with encephalitis if the infection spread to the brain parenchyma. And then inside the brain parenchyma if we have a walled off infection we call it a brain abscess and if it is not walled off by a capsule we call

it *cerebritis*. And all of these could be accompanied with suppurative thrombophlebitis.

Symptoms include fever and headache in almost all of them. In meningitis we expect neck stiffness and meningeal signs. And in other space occupying lesions depending on where the lesion is we expect the symptoms, we expect focal neurological signs and symptoms of increased intracranial pressure.

In the case of meningeal signs we do CSF analysis by lumbar puncture after we make sure there is no increased intracranial pressure.

But if we don't have meningeal signs, if we just have headache, fever, and focal neurological symptoms like confusion and so on we suspect other focal suppurative infections.