OPHTHALMIC MANIFESTATIONS OF SYPHILIS

Speaker: Ronald Plotnik, MD, MBA

10/26/2016
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[video transcript]

[00:00:08] Thank you very much for having me. It's my privilege to able to speak with you. We do see Syphilis. We see a lot of Chlamydia.

[00:00:18] We don't see very much GC. But, syphilis is, in the eyes, a serious disease that when we see patients where there are symptoms suggesting it, we actively test for this, so we test a lot.

[00:00:33] Next slide please. The objectives here are to recognize key points in the history, physical, and non-ophthalmologic ocular exam, which would suggest syphilis, and to gain awareness of sexually transmitted ocular disease. Primarily, I'll be showing you slit lamp photographs of patients but with the orientation towards what you'd be able to see with a flashlight looking at a patient without a slit lamp.

[00:01:09] Next slide please. So, you're all familiar with syphilis, the etiologic agent is Treponema Pallidum. Next slide please. Just as a very quick summary of primary Syphilis, characterized by the initial lesion appearing two to six weeks after infection. Secondary syphilis, occurring for 10 weeks after infection with non-specific symptoms; fever, malaise, and a rash especially on the palms and soles. During primary and secondary syphilis, if you look at CSF trying to find Neurosyphilis, you often find findings but with primary and secondary syphilis you need to have systemic symptoms in order to pursue CSF evaluation, and we're going to talk more about that. So, tertiary syphilis is neurologic but primarily cardiovascular manifestations. Latent syphilis, is clinically undetectable syphilis that can persist for many years. And what I do want to stop and spend a little bit more time with his Neurosyphilis. Neurosyphilis is important because that's what's associated with ocular involvement. Next slide please. So, this occurs when T. pallidum invades the central nervous system. It can occur at any stage early or late. So, it can occur during primary, secondary, tertiary, or latent. The ocular findings, or findings of neurosyphilis, can be asymptomatic. It usually occurs within a few months to a few years after infection but it can occur up to many years out. The clinical manifestations, in terms of neurosyphilis, there is more acute manifestations and more chronic. You can have cranial nerve abnormalities, meningitis, stroke, altered mental status,

[00:03:10] auditory issues, loss of vibration sense, motor deficits, other sensory deficits, and then the ocular involvement. So, the reason I want to spend time here is that neurosyphilis and ocular involvement are they're sort of in the same category. Treatments are the same. There is a lot of things that these two entities share in common. Next slide please. So, this is just a slide showing, on the left and the right, the area of light signal density on these scans showing areas of central involvement, brain
involvement. So, when we see a patient with ocular involvement we’re thinking neurosyphilis. And so, there are indications for cerebral spinal fluid evaluation through an LP, lumbar puncture, and so really it's it's patients who are more likely to have neurosyphilis or ocular syphilis or those who show symptoms. So, in primary and secondary, you don't get a CSF evaluation unless there's neurologic or eye symptoms. If there's tertiary syphilis, then that alone, even without eye findings or central nervous system findings, that's an indication for CSF evaluation. Treatment failures and significant HIV infection are also indications for CSF examination. And just to reiterate, the eye findings alone are, for us, the main indication for referring for CSF examination. Ok, I want to talk a little bit about eye anatomy so that what I'm saying kind of makes sense, hopefully. On the left is a cutaway of the eye and going from left to right you see the cornea, which is the clear watch glass surface. Behind that is the lens that's what you see is that disc shaped structure and between those two structures is a clear space. Does that work?.

[00:05:46] No

[00:05:48] Okay, well I'm sorry, I apologize. But, there is a there is a clear space there, right? And on the left in the same place, Ok. And that's that's an important space because when we look at the eye at the slit lamp, that's where a lot of the action is. As you go further back, the retina lines the inside of the eye and then you have the eye wall, or the sclera. But, for syphilis, the action is in the vascular layer between the white ocular wall in between the sclera and the retina. It's in the vascular which goes all the way forward and includes the colored iris. So, that tissue, the colored iris, goes back as a vascular layer all the way around the eye. Yes. I apologize if it's not large enough. So, when there's inflammation of that layer, of the iris, and as it moves back it's called the Pars Plana or further back it's called the Choroid. But, as that layer is infected with syphilis you can see inflammation either in the front of the eye, in the middle of the eye, or the back of the eye. And so, we categorize that as either Anterior Uveitis, Uveitis is inflammation of that tract. Intermediate Uveitis in the middle or Posterior Uveitis. Syphilis can affect any of those structures. It's more serious the more posterior in the eye that you go. So, the case definition for Ocular Syphilis is a person with clinical symptoms and signs consistent with ocular disease and uveitis, and Panuveitis is when all of those layers are affected, with symptoms including decreased vision, swelling of the optic nerve.

[00:07:46] There's a whole list of things, all of them have "-itis" on the end of them. They're all inflammation of ocular structures. And for anyone who has any ocular complaints and syphilis at any stage, they need to be seen for very urgent, maybe not immediate, but within a day or two, ophthalmologic exam; and the vision is down it becomes much more immediate. The infection can lead to blindness and when we see patients with inflammation, we are always thinking about this because it's curable, we can usually figure out what it is, and treatment is typically fairly effective; and then it's usually associated with neurosyphilis as I've said. So, there is a series of pearls and most of these are really from the CDC update on syphilitic ocular disease. And so, I'd like to just go through them before I
get to the photos of the actual ocular findings. So, clinicians should be aware of ocular syphilis and screen for complaints in any patient at risk for syphilis. So, have you had any decreased vision, red eye, light sensitivity, something to indicate infection within the eye. All patients with syphilis should have an HIV test. Patients who are positive serology and early syphilis without ocular symptoms should have a careful neurologic exam. Next slide please. And then, we talked about the CSF exam. So, anyone with ocular syphilis needs a CSF exam. And then, the treatment for ocular syphilis goes along with the treatment recommendations for neurosyphilis; not with primary, secondary, or tertiary syphilis. And that includes Aqueous crystalline penicillin g IV

[00:09:47] Or a combination of Procaine penicillin IM with Probencid, and then, in addition to that, they need treatment which would be for late latent syphilis which is 2.4 million units of Benzathine penicillin IM once a week for three weeks. So, the treatment has two part if the eye is affected. Next slide please. There are two tests that we all got they’re non-treponemal tests and treponemal tests. We get these tests all the time because any patient that comes in with ocular inflammation, we we work them up and part of our work up is these tests. The non-treponemal tests, the VDRL and the RPR are the primary ones, are both qualitative and quantitative. They reflect both disease activity and response to therapy can be tested used to test for reinfection but, have low sensitivity and specificity. And these measure antibodies directed against Cardiolipin-lecithin-cholesterol host antigen, so they’re not direct, it's not a direct test. The Treponemal test, the qualitative tests, there are a variety of them. The classic is the MHA-TP. There's the TP-PA, there is FTA-ABS, and then the EIA and the CIA. So, these are sensitive, usually reactive for live. You cannot measure titers to indicate response to treatment or severity and it's a it's a direct antibody specifically directed against T. pallidum antigen. So, for us, the bottom line is is that you need to get both tests, you need to get one of each test because one is sensitive, the other is adds additional information. But, each test alone doesn't tell you whether the patient needs to be treated. Next Slide. So, there is this reverse sequence testing recommended by the CDC.

[00:11:59] And it makes sense and it can really distinguish between those needing treatment, those who have been treated before, and what it does is it starts on the top with a treponemal test. If that treponemal test is negative, you're done. They don't they don't have syphilis. If the treponemal test is positive, then you do a non-treponemal test. If the non-treponemal test, the RPR, is positive, then they have syphilis. If it's negative, you do another treponemal test. And you'll notice, I mean it starts with the treponemal test. I don't know what your practice is but like with our residents they tend to reach first for they RPR or the VDRL and not with a treponemal test. And, at least in our setting, because we're worried about latent syphilis and neurosyphilis, I don't think that's right. I think we should be starting with a treponemal test. Next slide please. So, in terms of ocular syphilis, this is just a list of those "-itis's". Which is pretty much every part of the eye with "-itis" attached to the end of it meaning inflammation, because it really can affect any part of the eye. And I'd like to try to direct my talk at least the beginning of this part towards what you would see with a pen light. As we get to the retina, you are not going to be able to see any of this but I thought I would just give you an idea of what we're looking for. Next slide please.
So, let's let's go to the front of the eye. The conjunctiva is the clear layer over the white. There's another clear layer between the conjunctiva and the white sclera called the episclera and then the white of the eye. And so what we see here is what we call a follicular reaction of the conjunctiva. So the conjunctiva lines the White of the eye, but it also was lines the inside of the lids and, I don't know if you can see it there, but but there's little bumps all across the inside of the upper lid. We flipped the lid and were looking at the inside of the lid. If we look at a light reflect, for the light is reflecting off the surface of each one of those bumps, you can kind of get a feel that those are that there's a bumpy surface. And those are actually follices, they're individual collections of white blood cells. That's not specific for syphilis, but it's something that we look for. Both of these slides are episcleritis so that that middle layer between the conjunctiva and the sclera being inflamed. And so, on your left, there is a diffuse episclerites where all of the episclera is affected. And on the right we see what we call nodular episclerites where it's a very focal place but that, it's difficult to tell in the picture, but that area is elevated. There is thickening and swelling of the episclera in that region. Next slide. This is another picture of episclerites, little more severe, and maybe, if you look at the bottom part it's a little redder,

so it may be that we're getting into inflammation of the sclera itself down below. You'll also notice, perhaps, that around the clear cornea on the upper part there's sort of a ring of red that's sort of circumferential around the base of the cornea. That is a sign indicating that there is inflammation inside the eye. It's called Ciliary Flush. And I think I have another side of that. These are both sides of sclerites. So, it just you didn't even if you've never seen this before, you can see it looks pretty severe compared to the more superficial infections. This is an inflammation, this is actually inflammation of the eye wall that can lead to thinning and even perforation of the eye wall due to the infection. The one on your left is more focal, the one on the right is more diffuse, but both are very serious. Now Iritis, patients think it's e-y-e "-itis", but it's i-r-i-t-i-s, is inflammation of the iris which is the anterior portion of that vascular layer. And when we don't typically see inflammation of the iris itself, we see the effects of the inflammation. And so, we see collections of white blood cells at the pupillary border, we see collections of white blood cells in the back of the cornea, we see scarring in the eye, and you'll notice that that ciliary flush, that I mentioned before, is present here. So, the redness is really very concentrated in a circle around the cornea, and so this you would be able to see with a pen light. Next slide please.

So, this would be hard to see with the pen light but with a slit lamp this would be very obvious and those white spots on the back of the cornea are collections of white blood cells due to inflammation inside the eye. Sometimes the insulation is so severe that you can get what's called a hypopyon, where the white blood cells layer in the bottom and they're actually you know liquid; when patients lie flat it then you know spreads out and then when they're upright it settles down to the bottom again. But this inflammation is stuck to the back of the cornea. And the collections of white blood cells are large and so we call that granulomatous. And granulomatous inflammation like this very limited syphilis, sarcoid, few others. So, when we see the large collections like this we know how to direct our lab work up. This is a good picture of ciliary flush, I wanted to make sure I got a few of them in
there because it's really the main thing that one can see looking with a flashlight where you'd say you know, that is not just pinkeye, that is something inside the eye and more serious.

[00:18:00] OK. So, what are we looking at here? Well, the iris you can see is irregular and what it is is due to inflammation.

[00:18:08] Fibers tissue has adhered the back of that iris, that vascular layer, to the lens behind. The lens is supposed to be you know sitting behind there and not attached to the iris and here we see what kind of looks like a cloverleaf iris. This would be visible with a pen light and this is indeed indicative of a lot more long or standing infection. So, even if the eyes not red, if they have this they most likely had a previous bout of intra ocular inflammation. This is another picture where we see the front of the lens where the iris was stuck to the front of the lens and then we dilated it with drops and, except for that little area down below, it pulled away from the lens left some pigment on the lens surface. This is this is sort of a combo shot where we have scarring, we have inflation in the front of the lens, we have those precipitates in the back of the cornea,

[00:19:05] And this is this is a very classic picture for syphilis.

[00:19:16] What this is, if you can see those little dots floating around in the front of the eye, it's a difficult picture to get, but those are clumps of white blood cells floating around in the area behind the cornea and the fluid behind the cornea but in front of the iris due to inflammation of the iris. And what this is is a very narrow beam shined in the eye from your right to left where you can see the two bright areas, that's not the problem, the problem is in between those bright areas and all those little tiny dots are clumps of white blood cells floating around the anterior chamber of the eye. Ok, this is now two different types of pictures of the cornea. So, you should be able to see through that clear watch glass cornea to see the iris. You can see on your right you can't see through because there's scarring of the cornea, and if you look within that whiteness that's scarring you can see blood vessels all the way around and that is also very classic for syphilis. If you look at the red reflex on your left, like a cat eye reflex, you see the the red the light coming out, it's red because of the retina, but you can see it outlines the blood vessels that have grown into a different cornea then on your right, and this is a case of it's called interstitial keratitis due to syphilis. The left sides hard to see we'll just go to the right.

[00:20:43] You can see that there were blood vessels there the blood vessels are no longer there but there's scarring around the blood vessels and it leaves what we call ghost vessels. Where you can see the remnants of the vessels, but the vessels themselves don't have blood and are not active and that's also fairly specific for a few things including syphilis. One thing syphilis can do, especially with trauma, is there are these little strains that hold the lens in place, they can be weak. And so, what you see in both
of these pictures is the lens, if you look at the left it's supposed to be behind the iris not in front of the iris, and you're not supposed to be able to see the edge a lens, where it's come forward and down. On your right you see that the lens is going off to the side. You should not be able to see the edge of the lens, it should be behind the iris. So, dislocation. The other thing is this is this has that posterior scarring like we saw before, but you can see a cataract. So the lens instead of being clear has become cloudy due to the persistent inflammation. And again, these are patients with syphilis where they've developed a cataract, where the iris is scarred, where there's peripheral corneal involvement, and inflammation in the front of the eye. Now, this is the these findings you're not going to see with a pen light but, I thought would be of interest. So, the choroid, the uvea tract that the posterior extension of that vascular layer, becomes infected

[00:22:17] and it affects the retina overlying it. So, when we look in the eye we can you can see the retina sometimes you can see that vascular layer behind it. But, you can see here all those white dots, especially the larger ones, those are all parts of an acute syphilitic retinal and choroid infection.

[00:22:38] This is another slide where the infection has been there for quite a long time and we see loss of pigment, loss of retina, you can still see the the blood vessels in the retina going through that area that's de-pigmented.

[00:22:53] But, that's what there's no retina to see. So, there's visual loss associated with that lost retina. These are two other cases, the white spots on the back are active sort of clumps of infection in the choroid, in that vascular layer, and the overlying retina which would be fairly obvious with our headlight exam but not even with the hand-held direct ophthalmoscope. These are hard to see that way but they're easier to see with a wide field view. So, this is not something that you know you, even if you knew how to use a direct ophthalmoscope, that would be very easy to see. And this is late syphilis with loss of retina in the upper left. The other photos are it's an angiogram where you can see that there is the white is blood. And blood flow and so all those areas of black are lost vasculature due to the scarring from syphilis. And in another case where more extensive retinal involvement, this is an active infection that you can see it's kind of creamy white that's, indicative of the more active versus in old infection. And if you look on you're right, where the optic nerve comes into the eye, it's supposed to be a little nice circle where the nerve comes and it looks very elevated and I'll show you one other just coming up very quickly. Next slide, please. OK so here is again all the white that you see in the back is not supposed to be there.

[00:24:29] These are normal optic nerve so you can see you know the optic nerve is where the blood vessels are coming out of it's where the revision comes into the eye and it's a nice round, crisp circle, so it has not been affected in this case. Next slide, please. One of the things that can happen is you can have the blood vessels infected. And what we see is an angiogram on the left where blood is leaking out
of those inflamed vessels and on the right you can see a lot of hemorrhages that can occur with that retinal infection. Again, hemorrhages from the retinal infection, scarring, the area on the left is acute the area on the right is chronic. Up above we see a retinal detachment where fluid has accumulated between the retina and that layer behind it pushing the retina out and off the back of the eye. This can result in complete visual loss if it continues to detach and the retina ends up really in the middle of the eye instead of up against the eye. Wall.

[00:25:34] This is a case of late, complete retinal detachment,

[00:25:39] where the retina has scar has come off and scarred, and rather surgeons actually operate on these to put it back on, but it's very very difficult. You can get a condition called a acute posterior placoid chorioretinopathy which is just a lot of mumbo jumbo for coin shade lesions in the choroid in the retina due to infection. Sorry to go so fast I just want to make sure I get through these. This is an area where the middle of the eye is affected and we call these snow banks down below where there are collections of white blood cells in the middle of the eye. OK, on the left is a normal optic nerve, on the right is an optic nerve where syphilis caused an optical neuritis, inflammation of the optic nerve, and this is the nerve late where there's complete pallor of the nerve, more so on your left then the right. But, some of these patients see well but some of them see extremely poorly. And the last thing I just wanted to touch on is there is a pupillary abnormality that you can see with syphilis called an Argyll Robertson Pupil. Normally, when you shine a light in the eye, the pupils get smaller. When you go to read, or look at something close, the pupils also get smaller. And in this condition, the pupils react to near, but they don't react to light. And that's called an Argyll Robertson Pupil.

[00:27:09] Thank you very much.

[end]