Case Discussions

National HIV Curriculum Podcast

Evaluation of Focal Neurological Symptoms in a Patient with Advanced HIV

April 2, 2024

Season 1, Episode 7

National HIV Curriculum Podcast Editors Dr. Jehan Budak and Dr. Aley Kalapila discuss an approach to working up a patient with a CD4 Hello everyone. I'm Dr. Jehan Budak from the University of Washington in Seattle, and welcome to the National HIV Curriculum podcast. This podcast is intended for health care professionals who are interested in learning more about the diagnosis, management, and prevention of HIV. I'm back with my colleague Aley Kalapila, an ID physician at Emory University in Atlanta. Hi Aley.Dr. KalapilaHi Jehan. Hi everyone. Looking forward to yet another opportunistic infection podcast.Dr. BudakGreat. So, today we'll be talking about a case where the patient has focal neurologic symptoms, which is always a worrisome finding, and we're going to be touching on some points we discussed in our prior podcast about the evaluation of a patient with advanced HIV and headache, but this time we're taking a slightly different direction. So, let's get started. Dr. BudakSo this case is that of a 27-year-old man with HIV who presented to clinic with a subacute headache that began two to three weeks ago. His headache is mild, diffuse, worse with any movement, and has been worsening to the point that he has nausea, vomiting, generalized weakness, and dizziness. He denies fevers or chills, changes in vision, chest pain, abdominal pain, or diarrhea. He was started on ART [antiretroviral therapy] a few years ago but has been out of care and off medications for several years. Two years ago, his CD4 cell count was 90.On social history, he was last sexually active with a man a year prior. He was born and raised in Atlanta and has had no travel outside of the U.S. And then on his exam, he's afebrile, hemodynamically stable, appears cachectic. His speech is slowed, mildly dysarthric. His cranial nerves were intact, but he had slight decreases in strength on the left. He had dysmetria with finger-nose-finger bilaterally, worse on the left, and difficulty with rapid alternating movements, again, worse on the left. He had a broad-based ataxic gait, and negative Romberg, and no pronator drift. Dr. BudakSo, Aley, what were you thinking about or what are you thinking about right now?Dr. KalapilaYes, so there are a lot of things going through my mind when I see a patient like this with these kind of symptoms. So first off, I'm always going to check what his CD4 count is. So, in this case, his CD4 count is low because the last one that we had from a few years ago was already less than 200, and he has been off of antiretroviral therapy for the last

several years. So, we can safely assume that his current CD4 count is very much going to be less than 100. Now, with that low CD4 count, his clinical symptoms of a subacute headache, and his exam findings; that, to me, are pointing towards cerebellar dysfunction. I do think that there's something here that's causing focal neurologic deficits.And so, in this patient with a low CD4 count, the things that I would think about would be something that's causing space-occupying lesions. And so this could be toxoplasma, which we often refer to as toxo, primary CNS lymphoma, brain abscess. But given that this is the evaluation of a patient with advanced HIV/AIDS and subacute headache, I don't want to anchor. I want to keep my broad differential here because he could be at risk for multiple things. And so other pathogens that I would consider in a patient like this would be cryptococcus or even neurosyphilis, for instance, too.Dr. BudakSo you've got this broad differential, what do you want to do first to manage this patient?Dr. KalapilaSo again, given the headache and the focal neurological findings, I would 100% want to start off with a non-contrast head CT to look for any gross abnormalities. So the things that I would be looking for would be a mass, maybe signs of edema, signs of increased intracranial pressure (or increased ICP), brain hemorrhage, for example. Now, if the CAT scan doesn't show any acute pathology that would explain his physical exam findings, then the next thing that I would want is a lumbar puncture. And I would also actually consider getting an MRI, just given the focal neurological deficits. As well, I think the MRI does a better job of visualizing abnormalities in the brain parenchyma.Dr. BudakOkay, so the stat non-contrast head CT is obtained. And let me share the read. Well, my interpretation is that it's very abnormal. It has multifocal densities in the brain parenchyma, diffuse vasogenic edema, and significant midline shift. So, based on that midline shift, an LP [lumbar puncture] would not be safe.Dr. KalapilaYes, you're absolutely right. There was no way we would be able to do an LP on this patient safely based on those CT findings because of the risk of brain herniation. And, I think this was a great point to emphasize here: that in a person like this with this low CD4 count, it is always advisable to get that brain imaging prior to performing the LP because you really want to know is it safe to do that LP? And in this case, it wasn't.Dr. BudakYep. And then when I looked at that CT scan, to my non-radiologist eye, I could very easily notice the midline shift and that the left ventricles were no longer visible, but the parenchyma was not super abnormal to me. And I guess, really, for me, it was a little bit difficult to visualize exactly what was going on in the parenchyma.Dr. KalapilaYou know, I completely agree. I looked at that CAT scan, and I was like, well, this is an abnormal looking CAT scan, but I don't exactly know what's happening in the brain parenchyma. There's a midline shift. I'm not going to do that LP. I was able to see that shift like you, but beyond that, I wanted to really get at what is happening in the brain parenchyma. And so this is the reason why I wanted an MRI with contrast.Dr. BudakAnd that MRI showed multiple ring-enhancing masses with midline shift of five millimeters, cerebellar herniation through the foramen magnum, and severe mass effect on the fourth ventricles and brainstem. And I remember looking at this MRI and was just taken aback by how abnormal the parenchyma was as compared to that initial CT.Dr. KalapilaYes, it was an extremely impressive looking MRI. And again, another great learning point here for people listening is that the CT is a great first step, right? It's a fast study. It's actually much more inexpensive than an MRI. And so there's a good reason why in the emergency rooms, the CT scan is often the first study that people do to rule out any acute neurological pathology, so things like hemorrhage, large masses, or calcified lesions. But, the bottom line is that the MRI is actually a more specific and sensitive study compared to the CAT scan, and so, in an ideal world, would be the more preferred technique if it was available. Now, the opportunistic infection guidelines actually do comment on this. They state that the MRI brain should be obtained in patients with equivocal or negative CAT scan. So, if the CT study was negative, you would go to the MRI because the bottom line is you're going to be able to better visualize any anatomic abnormalities on an MRI.Dr. BudakSo with these MRI imaging findings, what do you think is going on?Dr. KalapilaPutting this all together. So again, multiple ring-enhancing lesions in advanced HIV, in my mind, is toxoplasmosis (or toxo) until proven otherwise. Now, we don't really know what his baseline serum toxo IgG status is, but if I had to bet, I suspect it will be positive. Other things that I would want to think about, again, trying not to anchor. When you think about patients with advanced HIV and contrast-enhancing ring lesions would be a primary CNS [central nervous system] lymphoma, and probably more rarely you could see a cryptococcoma or tuberculoma. And again, I know that we're anchoring on opportunistic infections on our differential right now because we're talking about someone with such a low CD4 count. But other things to think about that could affect everyone, including him, would be metastatic cancer, brain abscess, or even like a syphilitic gumma. But I think that would be extremely unusual.Dr. BudakAnd so, since an LP is contraindicated, what serum studies would you want to get in this scenario?Dr. KalapilaSo, I would want to start out with a CBC and a CMP, so a complete blood count and a

comprehensive metabolic panel because our patients can have a lot of cytopenias at baseline, and they can also have renal and hepatic dysfunction as well at baseline. And then, oftentimes, the antimicrobials, that we might be adding on that we would give to patients to treat opportunistic infections or other HIV comorbidities, can also cause bone marrow suppression, can also cause renal and hepatic dysfunction. So, I think it's a good thing to know where you're starting from at baseline. So that I would definitely get. Like we mentioned earlier, I would 100% want to get a serum toxoplasma IgG. Now, someone who has had a previous serum toxo IgG that's positive, that toxo IgG is going to stay positive for the rest of their life. If someone had a negative serum toxo IgG a few years ago, they can still seroconvert by being exposed to toxo.So, in this case, because toxo is on my differential, I want a serum toxo IgG. And then CD4 count less than 100, subacute headache, 100% I'm going to get a serum cryptococcal antigen (or a serum CrAg). And then, of course, syphilis can have a myriad of presentations, often known as a great masquerader, but will fully present with a headache. And so, I would also want to use our standard syphilis screening algorithm and do our syphilis studies as well. In general, though, I think the point to emphasize here would be that this is a patient with a low CD4 count, and so I want to keep a broad differential because the fact is that he is at risk for multiple opportunistic infections that can occur concurrently or at the same time.Dr. BudakAley, that's such a great point. That's definitely something I bring up with learners. That it's important to consider that multiple problems may be present at the same time in a person with such a profound immunocompromised state. In addition, I'd also like to add for the learners that although an LP was unsafe in this specific patient, one of the studies that you could still get if the LP was safe is a toxo CSF PCR, which, if positive, could help confirm your diagnosis, but if negative would not rule it out. And by that, I mean the CSF toxo PCR is specific but not sensitive. And I recognize that not every place has this, and so if you have it, it is an option. Dr. BudakHis syphilis screen and serum CrAg were negative and his serum toxo IgG, as you suspected, came back as positive. So, can you take us through how you're tying this all together?Dr. KalapilaSo, putting all of this information that we have available for this patient together, I believe that he has a presumptive diagnosis of toxoplasma encephalitis because we have a serum toxo IgG that is positive, and he also has a clinical presentation and radiographic findings that are fully consistent with toxo encephalitis.Dr. BudakSo taking a step back, Dr. KalapilaExactly. So, his CD4 count was less than 100, which is the level that's the cutoff below which toxo encephalitis typically occurs. He wasn't on any medications that provided prophylaxis against toxo reactivation. And then we have this MRI, right, that's showing us these classic multiple ring-enhancing lesions, some of which now have mass effect as well. So, to me, all of these features fully consistent with toxo encephalitis, and I would want to manage this patient by starting empiric toxo encephalitis treatment.Dr. BudakBefore we delve more into the treatment of toxo for our listeners just a heads-up that this is the first half of the podcast, and so I'm going to go over a few key takeaway points at the end. That toxo encephalitis can occur from reactivation of latent cysts in persons with HIV who have a CD4 count less than 100, who are not taking toxo prophylaxis medications. And that the diagnosis of toxo encephalitis is made presumptively based on the things that Aley took us through: clinical symptoms, characteristic brain lesions on CT/MRI, and a positive serum toxo IgG. And we'll talk about the principles of toxo treatment and what happened to this patient in our next podcast. Aley, thank you so much and looking forward to seeing you next time.Dr. KalapilaYes, looking forward to part two.Transcripts and references for this podcast can be found on our website, the National HIV Curriculum at