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Diagnosis and Treatment of Neurosarcoidosis

PRESENTATION AND TREATMENT OF NEUROSARCOIDOSIS

Sarcoidosis is a systemic disease most commonly affecting lungs, lymph nodes, eyes, and skin, but neurosarcoidosis is not an infrequent complication. Welcome to The Clinician's Roundtable. I am Dr. Leslie Lundt, your host, and with me today is Dr. David Spiegel. Dr. Spiegel is an Associate Professor of Clinical Psychiatry and Behavioral Sciences and Director of the Consultation/Liaison Services at Eastern Virginia Medical School.

DR. LESLIE LUNDT:

Welcome to ReachMD, Dr. Spiegel.

DR. DAVID SPIEGEL:

Thank you Leslie. Again, it's a pleasure to be here.

DR. LESLIE LUNDT:

It's been a while since I have seen sarcoid and I presume for our listeners as well. Can you just review it for us briefly please?

DR. DAVID SPIEGEL:

My pleasure. Sarcoid is a systemic illness of unknown cause which people may remember associated with noncaseating granulomas, although 90% of clinical sarcoidosis is manifested by the organ systems you mentioned which were intrathoracic lymph nodes, pulmonary involvement, skin and eye involvement. In terms of epidemiology, women are generally affected more than men, adults less than 40 are generally affected, and it's most prevalent in not only African-Americans, which I think most of us who are medicine remember, but also Swedish and Danish Americans. It's also common in that group as well.

DR. LESLIE LUNDT:

I remember Swedish and Danish people, any idea why that is?

DR. DAVID SPIEGEL:

Actually no, I don’t have any idea. I just think epidemiological evidence show that. I don’t know if there is any correlation to show between the 3 groups Swedish, Danish, and African-Americans, I have been finding tough to find any correlation.

DR. LESLIE LUNDT:

Now, how common is neurological involvement?

DR. DAVID SPIEGEL:

Neurological involvement would actually may perceive a diagnosis of sarcoid itself, has been reported to occur in anywhere between 5% to 10% of sarcoid patients.

DR. LESLIE LUNDT:

5% to 10%? So not uncommon.

DR. DAVID SPIEGEL:

No. Not at all. Not at all. Think about it, 1 of every 10 sarcoid patients can manifest neurosarcoidosis that's certainly something that psychiatrist and people in hospitals need to become at least somewhat familiar with.

DR. LESLIE LUNDT:

And what psychiatric symptoms might we see in those patients with neurosarcoid?

DR. DAVID SPIEGEL:

In terms of just epidemiologically with psychiatric symptoms, they will occur in a subset of neurosarcoid patients when there are parenchymal brain lesions if you would, so in that particular population about 20% of those patients will develop psychiatric symptoms primarily delirium and psychosis. Now that said, I will tell you that psychotic symptoms have also been the presenting feature of case of neurosarcoid when there is just meningeal involvement or hypothalamic disease.

DR. LESLIE LUNDT:

So, I am wondering when we see a patient, especially African-American or of Danish descent that in hospital that presents with a new-onset delirium when would we think about sarcoid?

DR. DAVID SPIEGEL:

Well, I think one thing we definitely do is someone who has hilar, you know, hilar adenopathy on chest x-ray and certainly chest x-ray is not uncommon. That's when this certainly would raise your eyebrows to start determine this as a possible case of neurosarcoid. Additionally, keep in mind that psychiatric illness generally doesn't, at least first onset, generally doesn't occur in older people, and by older people I am not insulting me, I hope, because I am over than 40, but certainly most psychiatric illness like psychosis, schizophrenia, or bipolar is going to happen in late teens or the 20s. So, psychiatric illness, at least first onset, is not an illness of your 40s, so if you start seeing someone who is psychotic, okay, in their 40s or even their 30s, you want to entertain that something else other than pure psychiatric illness. Now, to have a prior diagnosis of systemic or biopsy-proven sarcoid, that's going to certainly up the ante significantly in terms of your differential.

DR. LESLIE LUNDT:

Makes sense. Now, that brings up another question to me. Do these patients typically present de novo or do we already know that they have systemic sarcoidosis and the neurosarcoid is the new feature?

DR. DAVID SPIEGEL:

I would tell you, but certainly not the majority. I think most people will be surprised to know that a little bit over 30% of sarcoid patients will have neurosarcoid before the onset of systemic manifestations and about that same number of cases will have the development of neurosarcoid at the same time as their systemic illness, so we are talking about a fair number of patients who have either the onset before or at the same time of the development of systemic symptoms.

DR. LESLIE LUNDT:

Now, how do you make the diagnosis? You won't go and do a brain biopsy, do we?

DR. DAVID SPIEGEL:

No, well, so I tell you right now, you or I would and that's for sure, but I am sure you know, I would definitely avoid it. It's interesting the way you come up with the diagnosis of neurosarcoid. Certainly, you want to have the suggestive symptoms of neurosarcoid and I will tell you that psychiatric symptoms aren't the most common manifestations, but for instance cranial neuropathies are very common in patients with neurosarcoid, primarily the VII nerve, which of course is the facial nerve palsy. So, everything that resembles Bell palsy, go to start upping the ante. Additionally, the parenchymal brain lesion, which I did talk about occurred in about 50% of neurosarcoid patients, so an example of these may be hypothalamic involvement which can include endocrinopathy such as diabetes insipidus. They can have mass lesions and/or encephalopathy up to 10% of patients, which is another fancy neurological name for delirium. Mass lesions, believe it or not, I guess in the right hand, if you would, can be biopsied. So, if you biopsy a mass lesion, a tumor-like substance in the brain, then that could give you definitive diagnosis of neurosarcoid presuming you have the other clinical manifestations of the illness. However, unfortunately that usually isn't available to us, so what we need to do is go on a probable or high likelihood basis for neurosarcoid, so this would include one, the symptoms I just talked about with neurosarcoid with some type of laboratory support for CNS inflammation, so what might that be. Well, fortunately, we have MRIs so that's going to show an elevated uptake in the meninges or the

brainstem. We also have access to the spinal taps or lumbar punctures, which can show an elevated level of CSF protein or lymphocyte and so the other thing you want to do with this type of illness is to exclude alternative diagnoses and alternative diagnoses can include malignancies, metabolic diseases such as diabetes insipidus or even cerebrovascular disease. So, we are going to rule out other alternative causes, have some of this laboratory support, and have a clinical syndrome suggestive of neurosarcoid. That's a good way to kind of rule it in and that's the way I usually see them in the medical surgical ward with a probable diagnosis, but I will tell you that probable diagnosis is enough to treat a patient.

DR. LESLIE LUNDT:

I am not hearing any blood tests?

DR. DAVID SPIEGEL:

Blood tests are a little less specifically, the one blood test you can do is check for an ACE, which would be angiotensin-converting enzyme, so you can check that as I think the primary blood test that you can use. Other than that, everything has got to go to the CSF.

DR. LESLIE LUNDT:

Okay.

If you are new to our channel. You are listening to The Clinician's Roundtable on ReachMD, The Channel for Medical Professionals. I am Dr. Leslie Lundt, your host, and with me today is Dr. David Spiegel from Eastern Virginia Medical School in Norfolk. We are discussing neurosarcoidosis.

And David, once you have made the diagnosis of neurosarcoid, what do you do?

DR. DAVID SPIEGEL:

Well, the primary treatment is still going to be corticosteroids, but before we get into the corticosteroids, I will tell you it is definitely a mixed bag with respect to treatment versus side effects.

DR. LESLIE LUNDT:

Well, I am thinking here, here you have potentially a delirious psychotic patient and you are going to give him steroids. That doesn't seem like the greatest idea?

DR. DAVID SPIEGEL:

It's interesting because the way treatment works just the way treatment works in the 21st century is in principle there are no random controlled trials for the optimal treatment in neurosarcoid, so even though we use corticosteroids as the mainstay for treatment, the response rate has been as low as 40%, to one study that shows it as high as 90%. So, in and of itself they may not be the answer, so people also will start using the cytotoxic agents, methotrexate or azathioprine, which have a response rate of about 66% for those patients that don't respond to steroids and then there is the immunosuppressive agent, cyclophosphamide which is given intravenously, which can also be used for refractory neurosarcoid. Now that said, the other 3 ACE I talked about methotrexate, azathioprine, and cyclophosphamide can all cause delirium in and of itself and the question you asked which I went through my round about way of getting there is an absolutely steroids can cause mental status changes and I will refer the readers to a great, great study done, the Boston Collaborative Drug Surveillance Study, which is still referred to this stage and was done in 1972 and what that surveillance program did was what is the rate of psychiatric illness as a result of steroids and it's totally dose dependent. If you have someone who gets prednisone or prednisone equivalence of less than 40 mg per day, the rate is still pretty low of about 1%, but once you increase the dosage to up to 80 from 40

to 80 mg per day, it goes up to about 5% and then once you get above 80, it's about 20%, so again it is definitely dose dependent. Now, the most common symptoms of corticosteroids is depression and mania, so it's certainly not uncommon for a manic illness to develop, although depression seems to be somewhat more common.

DR. LESLIE LUNDT:

Now, in the little bit of time that we have left, can you give us just a quick case of patient may be that you have seen with neurosarcoid that's real life?

DR. DAVID SPIEGEL:

Yeah. I actually had a patient on this service about 2 months ago and like I said he had biopsy-proven sarcoid through I think pulmonary involvement and totally developed these manic type symptomatology where he had grandiose delusions, pressured speech, couldn't keep a conversation straight, and of course, at that time the person was in their 40s, and they were thinking the person may have had a bipolar disorder either and not neurosarcoid because well the guy has no history of bipolar, but the fact that he is manic and to see a manic patient, call a psychiatrist. As it turns out, the symptoms he had other neurosarcoid symptoms, primarily which wasn't picked up initially was a cranial nerve VII facial nerve palsy, so after I kind of picked that up on my neurological exam I did, and without any psychiatric history, I kind of felt this needs to be more considered in terms of neurosarcoid, and as a result, they brought the neurologist in and indeed, I think again it was a probable diagnosis because no one ever biopsied a brain mass or peripheral nerve or a cranial nerve, nerve biopsy was a probable diagnosis, so the patient was begun on corticosteroids. Now, taking that a step further like I said in terms of what steroids does actually made that great point, the patient's illness actually got worse, psychiatric illness actually got worse not the medical illness. The neurosarcoid, I am sure, was getting better, but he became significantly more manic and psychotic to the point where he had actually to be restrained. So even though he was on antipsychotics to treat the corticosteroid-induced mania, they still had to continue with because of the neurosarcoid. The good news is eventually both were treated and the patient was eventually released from the hospital in baseline mental health.

DR. LESLIE LUNDT:

So, clearly an example where a psychiatric needs to work with the whole team to help both issues.

DR. DAVID SPIEGEL:

Yeah, absolutely and fortunately, I have a pretty good relation with many of the consultant psychiatrists at EVMS and so they have no hesitance to call me and no matter what time of day it is.

DR. LESLIE LUNDT:

Unfortunately.

DR. DAVID SPIEGEL:

Well, also I have residents so they will take the late night calls.

DR. LESLIE LUNDT:

That's right. Well, thank you so much for being on our show today.

DR. DAVID SPIEGEL:

Again, thank you very much to have me. I appreciate it.

DR. LESLIE LUNDT:

We have been talking with Dr. David Spiegel of Eastern Virginia Medical School in Norfolk, Virginia about the presentation and treatment of neurosarcoidosis.

I am Dr. Leslie Lundt. You are listening to ReachMD, The Channel for Medical Professionals. Please visit our website at www.reachmd.com, which features our entire library through on-demand pod casts. Thank you for listening.