#256 Sarcoidosis

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SPEAKERS
Matt, Everyone, Mary Beth, Stuart, Paul, John

Paul 07:48
So I'm going to present to you all the case of Miss Sarah C. Otis. She is a 32-year-old woman she's presenting to her PCP following a trip to the ER last week when she was biking to work, she got her wheel stuck in a trolley track and fell off of her bike. In the accident, she had some shoulder pains as she went to the ER. The X ray happily didn't show any shoulder problems. But the ER doc told her that the plain film showed "bilateral hilar lymphadenopathy" which she almost certainly didn't know what to do with and told her to follow up with her primary care physician. On your initial history, the patient is not experiencing any shortness of breath, she has no trouble at all biking five miles to work. She's never had issues with syncope or palpitations or chest pain. During the visit, she just recapitulates the ER visit and says that she does have a family history of sarcoidosis. And so after hearing this and reviewing the notes, Miss. Otis' doctor, who will collectively be us, decides to do further workup and evaluation. But we need your help to sort of refresh us as to where to start. So before we even get going, I feel like this is oftentimes how sarcoid presents itself to us. So how do you how do you explain sarcoidosis to a patient? Because I'm not even sure I can explain it to another clinician at this point. (Laughter from Stuart) Why don't we start - Thank you, Stuart - why don't we start with Marybeth and then, John can help piggyback off for him for that

Mary Beth 09:00
Yeah, it’s a great question and we have to answer it all the time. Every patient comes in this is very common right that they have been in the emergency room had an abnormal chest X ray got sent to us to for further evaluation. Oftentimes they come in scared thinking that they might have cancer or something and they say what the heck is this sarcoidosis? So we tell them we say this is you know honestly, we don't really know all the details of what sarcoidosis is, we do know that it's some type of inflammatory condition some sort of immune system gone awry trying to respond to an unknown stimulus. But we don't know the cause. We do know that it most often affects the lungs of up to upwards of 90% of patients have some lung involvement such as such as Miss Otis, but it can affect any organ. And so we have to sort of do a survey of systems to understand where this inflammatory systemic disease is impacting patient. And so we start by telling the patient that we're going to sort out If they indeed have sarcoidosis, and then find out where it's living, and then find out if we have to treat it,

Matt 10:06
john, any anything additional you add any analogies and comparisons, things like that?

John 10:12
Sure. When I see a patient like this I, I agree with everything Mary Beth said, and I try to express to them that sarcoid can be a very mild disease, and it can be a more severe disease and stressing that we need to figure out is this indeed sarcoid? And if it is, do we need to treat it? Do we just need to watch it, and also stressing that most patients get better from sarcoid? And so trying to reassure them that we want to be thorough, it's going to be a pretty big evaluation as we start, but not to be worried about that. We want to make sure we have the right diagnosis. We know the extent of the disease, and then we know Do we need to actually treat this disease. Go ahead, Marybeth.

Mary Beth 10:54
No, and I might add that, you know, I do, I do emphasize the unknown etiology of it. And I explained to them that I do have some understandings that something is triggering this, but it could be an environmental experience. So I explained I, for example, I use the example of the World Trade Center, where we saw an outbreak of sarcoidosis there. I talked about the possible infectious etiologies. I talked about that. It could be familial, as in this case, and I also talked about that oftentimes idiopathic and we can't really sort out how the patient got it, they often ask, how could I possibly have gotten this? I think that's the other important component of explaining sarcoidosis.

John 11:36
And the other thing I'll say to a patient is that it's almost like a callus you know that something is irritating and driving inflammation. And I just say a granuloma almost like a callus, I realize it's different. But at the same time, you have this sort of chronic irritation that drives formation of a granuloma, that irritation being the interaction of the epitopes, and the immune system.

Stuart 11:58
And john, for our audience, can you describe what exactly is an epitope, so that they have a common understanding.

John 12:05
So an antigen that's presented by the immune system by the antigen presenting cells via the HLA system to the CD-4 cells, so that drives the inflammatory process in sarcoid.

Stuart 12:18
And before we were recording, we were talking a little bit about whether you can treat that with antibiotics or not. And I just want to get your words on this so that our audience understands.

John 12:29
Okay, so there is some thought, you know, Marybeth touched on the fact that sarcoid can be driven by exposure. So beryllium, I had a patient recently with cubic zirconium exposure through work. And but also there's a thought that it can be triggered by recognizing commensal organisms, and the two main

ones that are thought to be driving this intubated in the sarcoid world are proteobacteria, acnes, right. And Mycobacterium species, and there are a lot of Mycobacterium species, and we can't culture them all. And there's some part of those species that's no longer a viable organism that's being presented via HLA system to the immune system. And instead of being ignored, as it should be, or recognized, and then saying, "This is not a threat" it is being reacted to so that we think is the driver behind sarcoid, whether it's beryllium or some other occupational exposure, or whether it's this unknown driver, possibly being one of those organisms.

Matt 13:33
I'd like to talk a little bit about the history here. So we gave you the history for Miss Sarah C Otis, and Mary Beth, are there any additional questions that that you would like to get like that are part of your typical history for a patient you're seeing that you suspect has sarcoidosis?

Mary Beth 13:52
Yeah, so I think that what we mentioned earlier, this is a systemic disease. So it's a multiorgan involvement. The questions that we ask, focus on finding out which organs are involved in sarcoidosis, so and the other questions we asked really are centered around understanding how severely the patient is impacted. So the history and physical we have is really very comprehensive. And I think that it's very helpful to clinicians to have some sort of templated note or some sort of templated checklist to make sure that they review every organ system that can be involved. And those include neuro-psych involvement, ` involvement, respiratory, which is the most common 90% of patients are so have respiratory involvement, but GI, liver, renal involvement, skin involvement, cardiac, etc. And I can go through each of the we can talk about those manifestations and each of those organs in more detail as we move along. The other thing is important to talk to them about potential exposures that could be causing this. And then the third element that I think is important in the history and physical is weeding out the mimickers of sarcoidosis. So I want to ask them about potential, fungal or AFP infections and having systemic manifestations that way, I want to ask them about their immune system. Specifically, how do they have a history of you know, recurrent infections or something that might make me think about an immunodeficiency that's driving this, I want to ask them about be symptoms that consider the possibility of the differential lymphoma. So asking them about fever, night sweats, weight loss, etc. And then, as I said, going through each organ system, I think that's john probably has some other thoughts, too. It's a very comprehensive history. So it's a long, it's a long history for that initial evaluation.

Matt 15:51
JOHN, do you do you use a - Is there a standard form or questionnaire that you have for the patients with sarcoid? as it were, is there something available publicly that our audience can use if they have a patient they're suspecting?

John 16:02
I mean, there are articles that can go through your workup and your history and sarcoid. I have a templated note that I use because I just can't remember. And I actually asked those questions every visit, really, I mean, you know, as I get to know, the patient, and I see the manifestations of their disease, I back off on what I'm asking about. So it's not such a lengthy visit every time but I at least sort of check the box that I'm reviewing, you know, are you having cardiac symptoms? Did you have

syncope? Did you feel like your heart racing? Do you have any focal numbness, you know, the really important things, you don't want to miss it sarcoid because it can affect every organ, like Marybeth said, and you just want to make sure you don't miss the ones that can cause real damage to a patient's life? And so I just have a templated note, to make sure I'm reviewing those things every time and it's pretty quick, you know, I try to keep patient on task, saying, let's just move through these questions. You know, I'll talk about these other things. But I just need to move through these organ systems and make sure I'm not missing something here today, that I need to evaluate for.

Matt 17:03
Yeah, maybe I was thinking, as you're saying that it might be helpful if you if you and Marybeth wouldn't mind, if we could, maybe we could, you could share a copy of your note or we could make some form of that as part of our show notes or like a deliverable for the audience. It doesn't have to be the exact but just something that they could potentially use to, to ask about these questions, or to remind them like a checklist or something,

John 17:26
I can certainly share my note that I have.

Matt 17:29
So when I was reading about this, Marybeth I, I noticed that it seems like it's there's a delayed diagnosis, oftentimes. Are there things that you think people miss that maybe? Are there ways we can do a better job of identifying this early? Are there common mistakes that you see made? like someone's been seeing their primary doctor, their general internist or family doc for? Maybe if you could give the audience like maybe how can we help you find these people earlier and get them to you?

Mary Beth 17:58
Yeah, that's a fantastic question. I, you know, I think that certainly the asymptomatic patients, such as Miss. Otis, at least at this stage of her disease, are difficult to pick up unless you Incidentally get a chest X ray. So these people, you know, I'm not sure you know, how we would pick them up earlier, other than to say that, you know, clinicians shouldn't ignore, you know, interesting, maybe, incidentally, read findings on chest x rays, in terms of symptoms, because 90% of patients have some sort of lung involvement, and quite a few of those will have, you know, actually symptomatic disease, I think it's very important to appreciate when a patient tells you, they're dyspneic to understand and evaluate that. And I think a lot of times, it's easy for us when a patient tells us their dismay, to say, Well, you know, or even the patients do it, I'm out of shape, I gained weight, you know, I'm getting old things of that nature, but to really query patients about that shortness of breath, and consider additional workup and that workup might include pulmonary function testing to pick up either restriction or obstruction, imaging where we might pick up some of the earlier findings of sarcoidosis, listening to the patient. So patients for example, with fibrotic sarcoidosis will have crackles. And you can hear that. So I think just paying good attention to someone saying that they're short of breath and working that up rather than just dismissing it would be a valuable tool in picking this up earlier. And because it's multi system to I think that patients that have unexplained rashes, unexplained red eyes, unexplained dyspnea, I mean, syncope or palpitations, these all deserve further workup to because these are also manifestations of sarcoid. And rarely high calcium and up beings are quite so patients with high calcium should also be considered for

the sarcoid evaluation. But I think if I had one sort of pearl is to just pay close attention when people say they're short of breath and get a little further evaluation on that.

Paul 19:56
Is cough typically part of that pulmonary presentation too or is it primarily dyspnea that patients Report.

Mary Beth 20:01
I'm sorry, oh, yeah, cough Exactly. And cough goes in that same category. So someone that has a chronic cough, that you can't explain, so it isn't post-viral, or it isn't, you know, the ACE inhibitor or something that deserves evaluation, very similar to what I mentioned, for the dyspnea.

John 20:17
I would add to that, that the delay in diagnosis, you know, it's you're never going to diagnose someone with asymptomatic, is 32, and it has adenopathy. But the delay in diagnosis of people who get multiple courses of antibiotics for something, you know, saying this is a pneumonia. And clearly, it's not responding to those antibiotics. And I see a real delay in diagnosis around that. And you see that in a lot of other diseases too. So just being aware that, hey, you know, in this clinical situation, I think this patient maybe has pneumonia, you understand that a primary care provider, or whoever saw the patient, ER doc, or anybody or me included, might think this is a pneumonia. But if you treat it, it doesn't respond appropriately to move on and to make sure you're not anchoring on that diagnosis. The other thing I'll add is, I feel like I see a fair bit of hypercalcemia with sarcoid. You know, it just and then I see kidney stones. And so someone who has stones, and you don't know why they're having stones, and then you know, you want to make sure that you're evaluating that person, what their calcium is, what their urinary calcium is, and could sarcoid be a driver for this.

Mary Beth 21:23
I agree with all of that. The other thing I would add, this is sort of to John's point about making sure you're not missing the dangerous manifestations. You know, I've seen this where cardiomyopathies that aren't worked up palpitations that aren't worked up syncope, pre-syncope that aren't worked up. These are, these can be presenting manifestations of sarcoid it should remain in your differential when patients present like this.

Stuart 21:46
Commercial

Paul 23:57
Well, sure. I guess I guess we should examine the patient. So, you know, you mentioned the crackles and sort of earlier Actually, I guess sort of related to ILD, Are there any other examination findings that again, sort of raise your antenna for sarcoidosis, or that or especially that especially tilt you in that direction, and why don't we Why don't we start with Marybeth

Mary Beth 24:15
Rashes. So you know that Yeah, certainly, we could show some typical rashes that you see in sarcoid. Perhaps, to go along with this. That would be something red eyes or something that I would pay

attention to, and peripheral neuropathy. So oftentimes, they'll have adenopathy in their cervical chain, or in their groin. So those are other findings on physical exam that could be telling you about sarcoid.

Paul 24:39
All right, john, anything else that we can impress our consultants with? Yeah, I would add that you know, the rashes can be pretty atypical looking like you want to think about erythema nodosum on the lower extremities. You want to think about their joints. Do they have synovitis? Do they have arthritis signs, on exam, then the neurologic exam too. I don't do it Detailed one, but more making sure they have adequate strength in all extremities normal strength and all extreme. So the exam is certainly helpful, but a lot of sarcoid patients you find normal exams as well.

Matt 25:14
Stuart, you're a big fan of ACE levels, right?

Stuart 25:18
Uhh, no? Am I supposed be?

Everyone 25:20
Laughter

Paul 25:22
for the purpose of this episode?

Stuart 25:24
Oh, yes, I love it, ACE in the hole. Yes.

Mary Beth 25:27
All right answer Stewart right answer.

John 25:30
Yeah, I'll take it. So the ACE level, the sensitivity is about only 75%. And there's specificity is also not good. So yes, it's going to be elevated in three quarters of your sarcoid patients, but it's going to be elevated in a lot of other diseases, you know, asbestosis, beryllium, coxy, diabetes, silicosis, TB, lung cancer, infection. So there's a lot of false positives there. And so we generally don't follow ACE levels, you know, for those reasons,

Matt 26:01
Marybeth for someone like Sarah. So, we have this what we think is asymptomatic sarcoid, it was picked up Incidentally, as the primary Doc, if you're the first person seeing her, before we refer her to you, or while we're waiting for her to get to get into see you. What sort of labs were additional testing, should we as a primary, just feel comfortable ordering.

Mary Beth 26:25

Um, I think you should order calcium to not to not miss a hypercalcemia, liver function test to make sure the liver function is normal and not and be the livers not being impacted by this. And also, that sets you up for treatment later. But in general, I think we need to move quickly to making the diagnosis. And what we need in this situation would be a biopsy and finding the pathognomonic noncaseating granulomas. So I would move quickly to getting that referral and getting that biopsy done. The other thing you could consider, particularly if the history is suggestive, is immunoglobulin levels to rule out immunodeficiencies which might be a mimicker of this as well. Of sarcoidosis when I say "this."

Matt 27:08
So that would be like the serum quantitative immunoglobulins

Mary Beth 27:13
Yep, yeah, I ordered. I ordered that. Yeah, IgG, IgM, IgA, and if you know, I have definitely found that what I thought might have been sarcoid was actually CVID. And then the lung manifestation of CVID, that's Common Variable Immunodeficiency, is granulomatous lymphocytic interstitial lung disease that can manifest by either lymphocytic infiltrates or granuloma infiltrates and can oftentimes look like sarcoid. So you know, just ruling that out can be helpful at the early stages.

Matt 27:44
Okay,

John 27:44
Can I ask Mary Beth a question? This is unprecedented. So, you know, this woman, she's 32, she has had adenopathy. If you did an EKG and you did labs, and you did a calcium, and you did a thorough history and physical Would you ever consider not biopsy seeing her if that was the only manifestation you had, because I see a lot of people with symmetrical adenopathy, and I don't see other manifestations and someone like her if it was only symmetrical adenopathy, I wouldn't put her on systemic therapy. And I might just follow her up in three months with a repeat image, and make and maybe repeat lab that make sure I'm not missing something. I'll make sure I'm not missing dangerous involvement of sarcoid saying, Okay, this may be sarcoid. If the adenopathy is not really large, and I'm not worried about lymphoma right now. And it's symmetrical and it checks all those boxes that it's likely to be. Maybe I just sit on this.

Mary Beth 28:41
Well, like all things in medicine and shared decision making, right? So you can talk to the patient. I mean, there are opposite. There are instances where we would talk to our patient and they would say, I'm not doing that terrible bronchoscopy, you're gonna waterboard me, you know, things of that nature. And then you can say that, well, that's a reasonable decision, because I think odds are this is sarcoid. Right? But I think I always worried about the differential of lymphoma, and I'm never comfortable that that's not it, and, and we have the luxury in Utah of not having a lot of histoplasmosis, but if you're in the middle of the country, this can be histoplasmosis, and you want to try to assess for that as well. And so if the patient's willing, I, I'd get a biopsy and I think it informs me down the line too, so I don't have to worry later. So if those lymph nodes grow, for example, oh, shoot, did I miss lymphoma, you know, you don't want to, you want to be pretty secure as you push forward. Or if the patient manifest symptoms

later to have that, you know, that biopsy in your pocket, let you move forward with therapy a lot quicker. So I prefer a biopsy early, but I agree with you. I think sometimes patients don't want to do that and are looking for you to reassure them that the odds are with them, so sometimes you'll make that decision for them.

Stuart 29:51
So my head's kind of spinning right now. How do we actually make the diagnosis then john?

John 29:57
Yeah, so I have a quote from an article, I think it was in the American Journal of respiratory Critical Care Medicine. And it said the diagnosis of sarcoidosis is arbitrarily made when the statistical likelihood of alternative diagnosis becomes too small to warrant further investigation.

Matt 30:15
Okay, so I just want to recap a little bit. So we've gone over, we're taking a multi system history, you all will share your templates with us. So that way we can put some of those questions that people should be asking systematically into the show notes. And we're thinking about the mimics of sarcoid. We're ordering just at the basic first visit for Miss Otis, we'd be getting something like a CBC because we're thinking lymphomas in the consideration CMP for liver, kidney involvement, we said a check of calcium. And we said quantitative immunoglobulins might be something we could consider. We talked about an EKG, and how we're still not certain that that's what she has john, that this is sarcoid. So how would we be very sure of the diagnosis? Because, yeah, well, let's just start there, then we'll have some follow up questions.

John 31:07
Okay. So we talked about how we think about the diagnosis is made by this arbitrary threshold. And so we want to take away the, from the differential, we want to exclude the more common mimickers. And so when we get a biopsy and someone like this, we would do an EBUS biopsy, we would make sure that her sample is sent for cytopathology, we would make sure that it's set for flow cytometry, make sure it's set for fungal and AFP cultures and states. And those would take away some of the common mimickers of sarcoid. Then when we're doing her lab work up, you know, we would maybe want to check a QuantiFERON gold, depending on risk factors, we would want to check an HIV, depending on risk factors. And so we want to take these other things where we think we're taking away the likelihood of that alternative diagnosis. And then we have a clinical picture, we've done our history. We've done our physical, we have our lab results, we have our path results, and does it all fit together, that we feel comfortable, fit together well enough, that we feel comfortable that we've excluded these other excluded common variable immune deficiency, excluded TB, fungal infection, and we feel comfortable that we've crossed that threshold that we can say, this is sarcoid. And now we can move forward with treatment of that. And I think even after we do that, if a patient then comes back and isn't behaving like you would expect to sarcoid to behave, not responding to treatment appropriately having manifestations that don't make sense. You don't have to ask yourself that question again. But for now, once you've done those things, you can move forward and say I've crossed the threshold where this is likely sarcoid everything else is very unlikely. Now can I can ask myself does it need treatment or not?

Matt 32:58
Paul, did you come across that in MKSAP this Lofgren syndrome, I'm sure everyone's come across this like, it sounds like that's the one time you know, Lofgren syndrome, which is the skin, the they have arthritis and the hilar adenopathy that will come up on boards that you shouldn't biopsy that person But Mary Beth, Mary Beth, in reality, does that person with Lofgren syndrome get biopsied?

Mary Beth 33:27
Not usually

Matt 33:28
Okay

Mary Beth 33:29
If you sent that person to a sarcoid expert or pulmonologist or rheumatologists, we would say this is pathognomonic for sarcoidosis does not need a biopsy.

Matt 33:37
Okay.

Paul 33:39
Any other slam dunk, homeruns, "this is sarcoid," we don't have to go after things with needles like any other presentations that are just so prototypic you feel confident in a diagnosis?

John 33:48
Well, there's Heerfordt syndrome right. It has uveitis, parotitis and fever. But my experience is that those folks generally end up with like biopsies of their parotoids. They get into ENT.

Matt 34:01
Don't they get nerve palsy is to is that that? That would always freak me out. Anybody that has nerve stuff on like, this. Yeah.

Paul 34:09
They're sent back from neuro. Laughter

John 34:13
I've seen the uveitis and parotitis. I've not seen the nerve palsy. Okay. I don't know if you have Marybeth. But the classic syndrome, I think, is those with fever. Okay. Yeah, got it.

Stuart 34:24
So getting back to Miss Otis, you plan to see her again after some labs and a non contrast CT of the chest. She leaves your clinic with an informational pamphlet on sarcoidosis. It's probably about 95 pages long. A few months later, you get a call from Miss Otis regarding her shortness of breath with exertion and a dry cough that she has noticed. She got busy at work and thus has yet to get the labs and CT done but now that she's feeling symptomatic, she wonders if this could be related to

sarcoidosis. So I'm going to go ahead and skip forward on the question because we've kind of discussed the alternative diagnoses. Is there a clear reliable association between In the radiographic stage of sarcoidosis, and how symptomatic a patient is when they present,

John 35:04
so no, there is not. I think in all lung disease, I've been really impressed with the degree of impairment that you see in imaging or in pulmonary function tests and the patient's symptoms. So you'll see a patient with sarcoid, who has pretty extensive parenchymal involvement, and they're really not symptomatic. And they can have preserved PFTs as well. And then you see folks who don't have that much parenchymal involvement, but they're quite symptomatic. And they may have impairment on their PFTs. And I think this is really complicated by other things. It's complicated by obesity. It's complicated by heart disease. You know, diastolic dysfunction, particularly pulmonary hypertension, and things that just don't show up on imaging. So, I don't think I think the imaging is really informative. I think the imaging is really important. But I think the correlation between what a patient is experiencing and what you're seeing on the imaging is not very good.

Matt 36:04
Marybeth, are you? Are you starting with a high res CT? And these folks like what sort of imaging be after the first chest Xray once they're symptomatic? What let's say they're not gonna be able to see you for six weeks, and we're the primary we want to get some imaging cooking, what might we order?

Mary Beth 36:21
Yeah, I appreciate that question. And I do think the high resolution CT scan is that workhorse of any interstitial lung disease and sarcoidosis included, you know, what you'll, what you'll be picking up there is whether there's parenchymal disease in addition to the lymphadenopathy that we saw in Miss Otis on her chest X ray. But oftentimes the, the parenchymal disease or the nodules that you might see that are classic for sarcoid may only show up on a high resolution CT scan. And the pattern on that high resolution CT scan is super helpful. So what you typically would see in circuit is these nodules, these tiny little nodules will be in this what so called peribronchovascular distribution. So there'll be kind of lumping up on the on the on the pleural spaces on the on the bronchovascular bundles, etc. And that pattern can be very typical of sarcoid and reassure you that that the diagnosis that you've made, is sarcoid. And that the findings on the lung CT scan are sarcoid. And then the manifestations that she's developing now with shortness of breath, are also classic for sarcoid and help you rule out those other differential reasons for her shortness of breath.

Matt 37:30
What if she had on her? I know PET scanning is something that sometimes people get so if she had heart block, is she buying herself a PET scan? Or what sort of things make you think this person needs a PET scan or I know cardiac MRI is another consideration?

Mary Beth 37:48
Fantastic question. So yeah, the PET scan can be helpful for a variety of reasons, a full body PET scan, in this diagnosis, sarcoid helps us understand potentially where the where the sarcoid is, so where we see inflammatory changes, either in lymph nodes, you know, outside of the chest, though, in

the abdomen, pelvic area, etc. That can be helpful. And then PET scans, you're asking questions more specific to a cardiac manifestation. And so when a patient has and as john has said, and I completely agree that we have to have a very high index of suspicion for cardiac involvement, and some of those manifestations may be, as you mentioned, an abnormal EKG or the patient may be symptomatic with palpitations, syncope, pre-syncope, or we may see actual, the shortness of breath could be the result of heart failure. So if an echo is abnormal, or the suspicion of heart failure, these are all reasons to suspect cardiac sarcoid. And then our diagnostic tools can include, as you mentioned, a cardiac MRI, or a cardiac PET scan, which is actually different than then a full body PET scan, the cardiac PET scan is really gated to look at the cardiac the heart tissue. So that's a that's a test that you can order as well. And yes, if she if she did have heart block, if she did have palpitations, she did by herself, the cardiac specific evaluation.

Matt 39:14
So john, while we're - Go for it

Paul 39:17
Sorry - John, I'll ask you while we're in the world of imaging. I feel like there's much ado made about the actual staging of sarcoidosis. Could you just talk us through that and what am I to do with that information?

John 39:28
Sure. So the staging of the pulmonary sarcoid is called the Siltzbach radiographic stages and, you know, we have stage zero disease, which really there's no pulmonary involvement. Stage one disease where you have just lymph node involvement, so mediastinal and hilar and that is present that is bilaterally. Bilateral. So if you have a unilateral hilar and unilateral paratracheal involvement, that would not be it. Stage two is when you get into parenchymal involvement and mediastinal and hilar adenopathy and the majority of cases present really in stage one or stage two disease. Stage three diseases where you just have parenchymal involvement and no adenopathy and stage four when you just have fibrotic. So that's that staging is important because it informs decisions. You don't have to memorize this the staging, but it's important to say, if someone has stage one disease, you know, I'm not putting them on methotrexate or steroids unless I have a good other reason to. So I'm going to stage two disease, well, then I'm really thinking about starting in a non systemic therapy, but I want to assess how much involved they have.

Stuart 40:43
Which kind of begs the question, What determines when you would start therapy for these patients? Is it the staging on imaging? Or is it symptoms or what what's kind of the trigger point.

John 40:57
So I think the trigger point, we think of damage to organs, that is progressive and irreversible, that may be occurring, or dangerous involvement. So people who are getting heart block, people who have neurologic involvement, so damage or danger being the paradigm that makes you want to treat somebody, if I have a patient, for instance, who is a young guy, very active, and he's losing some lung function, and he has quite a bit of parenchymal involvement, I'm going to treat that person, I don't want

them to be debilitated by progressive sarcoid. So you know, you have danger of losing more organ function and someone which can be, you know, quite a bit of morbidity that they are, if someone has involvement that's dangerous, they have neurologic involved they have cardiac, then I'm really going to move forward with aggressive therapy, and Mary Beth, as a primary care physician,

Stuart 41:51
Is this something that we need to consider doing before we send them to you if we're pretty certain about the diagnosis? Is it time sensitive, for instance?

Mary Beth 42:00
It can be it's not typically, you typically have time to secure the diagnosis so that you know you're treating the right disease. And so it's preferential to have that biopsy done. So you know, that you're treating sarcoid and not something else. And so I think it's, it's preferred to secure your diagnosis before you treat. Having said that, of course, patients, you know, the other john mentioned danger, but symptoms drive their, you know, the need to treat as well. And so when you're concerned about symptoms, sometimes, you know, you want to move that diagnosis along so that you get treating more rapidly. I don't necessarily recommend empiric treatment without a diagnosis.

John 42:41
Well, I agree.

Mary Beth 42:42
I'm sorry.

John 42:43
I was gonna say I agree with Mary Beth, sometimes you have folks you might not actually treat, but they have so many symptoms, and you're pretty sure they're related to their sarcoid diagnosis. And, you know, you treat them and try to limit the side effects of your treatments.

Matt 42:59
I think we should talk get back to Miss. Otis's' case here. It seems like she's now having symptoms. So Marybeth, let's say, it doesn't seem like she has a pneumonia, obvious pneumonia. She's not having fevers, we get a high res CAT scan, and let's call her Stage Two. What might you do for her? And what might that conversation sound like?

Mary Beth 43:26
So the conversation might sound something like - we're very comfortable with the diagnosis, this is your sarcoid that's treat that's acting, you're short of breath, I'm concerned about your symptoms, I think we should treat you. The medicines we have to use, all suppress your immune system in one form or another. The first line of therapy is prednisone. And, and we use that quite frequently. And patients are often very responsive to prednisone in sarcoidosis. And so we may want to start with prednisone to treat the patient. I tell them that. Typically, we don't need large doses to be effective. Oftentimes, we can start with something around 20 milligrams of prednisone, and that can help a patient shortness of breath. So I like to start on a lower dose, rather than giving them all the side effects of you know, high

dose prednisone. And so that I often will start with that. And then if they have a nice response, and we have difficulty, meaning it then we start moving into what we call the steroid-sparing agents that maybe John can tell us more about if you'd like.

Matt 44:29
Yeah, so just to throw the prednisone, you're starting at 20, hoping that that'll get their symptoms under control. And then you mentioned if we can't get them, you're saying if we can't get them under control, so you would keep them at that dose. If they do well then you would try to wean it down, but if they don't do well, you might start to add these second line medications.

Mary Beth 44:50
That's a that's a good strategy. Yes.

Matt 44:53
So john, what other medications would be your adjuvants to steroids.

John 44:59
Well, So what I would say is that if you start them on prednisone and they have a response, we want to taper that dose over six months. And if we can get that dose, under 10 milligrams, and they're stable, we may want to consider staying with prednisone as our medication choice. If you taper them down, you know, they have a nice response and then you try to taper them down. And then their disease flares, you know, they have a sarcoid flare, they start to feel worse, they get more, you follow up their CT scan they have now again, more parental involvement, then you want to move on to a second line drug. So I think, you know, understanding that prednisone may be the right drug, if it's a really low dose. If you can't control them with a low dose, then I think of methotrexate as the first second-line cytotoxic drug for sarcoid based on the amount of evidence available. And then there are a lot of other options along that pathway, which include azathioprine, mycophenolate leflunomide. There's a variety of drugs that you can use. But methotrexate is generally the one that you would start with as your second line drug.

Matt 46:09
Marybeth, do you tell patients, like for someone with stage two disease, like Miss Otis, would you tell her, there might be a chance she could come off all meds altogether? I mean, let's say that that's what she's worried about. In particular, she's just having a hard time she's blaming herself that she didn't follow up, like, could this have been prevented? Is there anything that could have prevented the progression from I guess she was stage one initially, and now she's stage two.

Mary Beth 46:37
Yeah, I tell her that, as we talked about earlier, that it's really hard to predict the course of this disease. And that, you know, some patients never need to be treated. Some patients, you know, it's about a third:third:third, depending on the series you read about. A third or more don't ever need therapy, the other third will need therapy, or maybe 50% and do very well and be able to come off of that at some point, the disease will either, you know, stabilize or actually fully remit. And a lot of patients, you know, in two years from now will have no further sign of their disease. And then some people need chronic

therapy, that that can we can control their disease with chronic therapy, and then a few people will sneak through the all the therapies we try to use in progress despite our therapies. But I would tell her with her sort of active looking inflammatory, you know, peribronchovascular nodules, that is clearly, you know, active and changing that we have a very good chance of controlling her disease either with the low dose prednisone that we talked about, or with a second agent. So I'd be I would be encouraging and reassuring, I think, and I think that would be appropriate.

Paul 47:49
Can I ask you both one of my typical vague questions, they'll be impossible. The answer will be "it depends". But I guess what I'm wondering is what is the treatment team for sarcoidosis typically look like? Like, for instance, at Kashlak northeast, I feel like it's sort of shared between rheumatology and pulmonology. And sometimes nephrology, depending on an involvement. Is this typically treated by a team with primary care as coordinator? Or is it usually run by pulmonology? Unless things get way far away from the lungs? What does the typical sarcoid team look like? If you don't mind me asking

Mary Beth 48:18
It's a great question. You teed us up for the very last question where you say, what's our advice and, you know, Dr. Boltax has done a very good job of actually developing a multidisciplinary team, and so that it does typically look like a large team of providers. Often the quarterback is the pulmonologist because as we mentioned, 90% of you know, sarcoid has some lung involvement, or rheumatologists because of the multi organ systemic nature of disease, but then we bring in experts, oftentimes, depending on your center, depending on who's available to you, that will help with the different organs that are involved. So if they have ophthalmological involvement - do you want me to pause? Can you hear that dog? I'm so sorry

Matt 49:01
No, it's okay. Like, we like pets on the show anyway, so that's okay.

Everyone 49:04
Laughter

Mary Beth 49:05
Okay, okay. So if they have ophthalmological involvement, we'll have an ophthalmologist who specializes in this. Cardiac cardiologists, etc. Dr. Boltax at the center of a multidisciplinary clinic at the University of Utah where several providers are in clinic together. So a patient can be seen serially by the value organ systems. And I think it's really important to remember that it's a high burden of disease for patients, right? I mean, they, there's a lot of uncertainty about the disease and the prognosis. And if they have multiple organ involvement, they may end up running around to multiple specialists. So the more we can help coordinate their care, to they're not having multiple visits and coordinate their care for the providers all agreeing on the treatment plan, the better it is for the patient. So I think we really try to encourage that sort of multidisciplinary approach to patient with a team, that that is all familiar with sarcoid and that they talk together.

John 50:01

And if I could just add, you also sort of develop your, your contacts within Derm, your contact within rheum, your contacts within. So even if you can't be in the same room, you know, you know that you want them to be referred to, you know who's in tune with what's going on with sarcoid. And it's going to understand what the needs are around to give the patient because it's hard to get, especially now with COVID, it's really hard to get everybody in the same room. And we have a great group of cardiologists, you know, neuro-sarcoid team, and we can all just bounce ideas off each other and have discussions, maybe not in the same room not seeing the patient same time, because that's just been so challenging. The other thing is your friendly neighborhood pharmacist is really your friend. Because these drugs, you know, you have to monitor drug toxicities, you know, dosing has to be adjusted. they are invaluable. So having a pharmacist on your team is just so important. And that's where I think it gets really hard for primary to manage this just from a resource standpoint. You know, imagine all the other things you have to do and then you're like, Okay, do I need to adjust their methotrexate because their creatine is changed a little bit? It's just really did I get their labs, am I monitoring labs? So that team, it would be impossible without, without a pharmacist on that team.

Matt 51:22
Before we make Miss Otis a little bit sick here, I wanted to ask Mary Beth, I have a fair amount of patients that I'll just be seeing them and I'll and I'll be looking in their history, and I'm seeing them for just the normal stuff, high blood pressure, obesity, whatever. And then I'm like, Oh, they have sarcoid. And they're not on any medications for that. And usually I think about like, do they need a dexa? Have they been? You know, do they have hyperglycemia related to having been on steroids? Where if they're still on steroids, but what things in primary care other than like getting them vaccinated, maybe getting them dexas as if they're on chronic steroids, anything else that we can do to help you all out, like in between visits, because sometimes patients selectively follow up with certain people, and they'll just let other doctors not see them for big chunks of time?

Mary Beth 52:13
I, you know, it's a great question. And I think what you do is you'd be that very good internist, that you are. Your, you know, doing a full review of system. And anything that doesn't quite ring true. You think of this, this sarcoid related. I think that's one important thing. I think you also bring up a very good point is that to understand what medications they are on currently, and what they've been on long term to understand medication side effects and prednisone is that number one, you know, drug that we oftentimes will neglect to take care of the potential side effects related to that such as high sugars, dexa, bone density, cataracts, you know, things of that nature. So I think that being aware that it's a multi system disease, doing a full comprehensive, you know, review the system, and being aware of their medications are the two really important, valuable tools that can help us with patients. The third thing I would say is being aware of, you know, steroid withdrawal, so patients that have been on prednisone for a long period of time and be taken away, for various reasons, say the pulmonologist that says you don't use anymore, then we leave them with adrenal insufficiency, internists oftentimes pick that up and help take care of that patient. And we should be doing a good job as sarcoid experts taking care of the PJP prophylaxis of patients on a dose of prednisone 20 milligrams or higher, should be on protection for that. But if your friendly neighborhood pulmonologist missed that that's something to pay attention to as well.

John 53:52
And I agree with everything, I just want to add one thing, I don't know, sarcoid just appears on people's past medical history, whether they've had it or not. I literally tried to pull like who in the university system had sarcoid and I reviewed 50 charts and I what I looked through those charts, I couldn't really find any evidence that they ever had an active sore, or that they were treated for sarcoid I think it just appears on

Matt 54:16
I thought it was just me

Everyone 54:18
Laughter

John 54:18
No, no. And I'm like, okay, that patient never had sarcoid So, the number one thing I would do is like actually ask myself Well, is there, really, did this patient ever have sarcoid

Paul 54:30
It is the blood stain on lady Macbeth's hands to like you cannot get that damn thing off the chart. Let's remove it and it shows back up like I have sent emails begging people, like please I beg of you stopped writing this down. It just ends up that it just gets backed up like a bad penny. It's amazing.

John 54:44
Yeah, sorry. And you I just I reviewed all their past medical history and I've reviewed every medication there.

Matt 54:52
Paul, why don't you take us. We're barreling towards the end of the show here. But I think Miss. Otis needs to get a little bit sick before - we got a we got to put her through it a little bit.

Paul 55:03
I mean, that's just good storytelling. We'll take her to the precipice and then bring the audience back. So Miss Otis has started on prednisone, we started on 40 milligrams daily. And over the next few months, she's tapered down to 10 milligrams daily. And she's doing okay on this dose. A few years now after your initial encounter, so she likes us well enough to stayed with us, you get a courtesy call from the hospitalist at Kashlak about Ms. Otis. Apparently, she's been admitted with respiratory symptoms. Upon further questioning, you find out that she's having shortness of breath, she has a new oxygen requirement. And she's having night sweats along with my allergies and arthralgias. And so I guess our initial question, why don't we start with Marybeth? Could this be a sarcoid flare? And could you also tell me what that is and what that means? Sure, it can absolutely be a sarcoid flare, but the differential is very broad. So you want to want to make sure you walk your doctor at Kashlak General through the, you know, the differential. Did you ruled out the pneumonia, et cetera, et cetera. Again, the high resolution CT scan or the CT angiogram, you know, that has pretty good resolution of the lung parenchyma is your friend. And so you look to make sure there wasn't a pulmonary embolism. And its

not heart failure, etc. And then if you see, you know, ground glass or more bronchovascular bundles or something of that nature, then you say, I think, yeah, this could be a sarcoid flare. And then we treat accordingly. Now, you asked what a sarcoid exacerbation is, it's essentially any sort of increased activity or the underlying sarcoidosis that, you know, that's been imbalanced, right? You've had this balance with either she's been in remission, or she's been on a nice stable dose of medications or not sure, in this case, which we're where we left her, but, and then the disease for whatever reason, has increased activity. So at that point, once you've ruled out your differential other causes, and you decide this is a sarcoid flare, then the therapy really is that, again, starting the prednisone at a higher dose, and then weaning that back down again, once she's in control.

Matt 57:06
Yeah, john, I think we had her on 10 milligrams or less a day at the start of this, this flare. So what might that look like in the near term? Just like a little bit more granular? Is it five days of higher dose and then back, taper back down? How would you do that? Typically?

John 57:25
I'm sure that that's, that's a good question. And the thing about this is you never do it exactly the same. Like, this is probably some of the frustration, there's just not a cookbook, you know, you'd want to know, well, how bad is her flare? What has her disease done over time? I mean, were her PFT's up until then, like, you know, normal and stable. And was her imaging normal or stable or was as you look back, you know, there was actually subtly increasing diseases this was going on. So I think what I would do is, I would probably put her back up to a level of 20 or more for, you know, not five days, but because this is a chronic disease for her but longer course than that, you know, maybe a couple of months. And if I really thought, Well, hey, this is, as I look back, and I take a really close look, you know, her disease has actually been a little bit active over this time, then I'd put on methotrexate as my second line drug and methotrexate takes a while to get up to steady state on the order of months, you know, four months or so. And so I would then slowly taper down steroids, as her methotrexate dose builds up, if she was truly controlled, you know, I might say, let's get you up on a higher dose for a month or two, let's see you back in a month and see what things look like, you know, is everything back to your baseline now that I got a month and then I'd kind of maybe more quickly taper or back down to 10. But it would never be the same every time. I mean, I just, they're so different, and the disease is so different, and every patient that you just have to adjust a little bit every time and that's the advantage of knowing that patient. Well,

Matt 58:59
and you hinted there that you would be following PFT's and imaging. So is that just like a high-res CT and PFT's is that once a year, every couple years?

John 59:09
Well, certainly some as a first make a diagnosis on somebody, I'll follow up in three months with repeat PFT's and maybe I can get away with a chest X ray, you know, if I have a high-res CT and then I have a chest X ray, I kind of know what those to look like. But you know, then a CT scan at six months. And when someone's first diagnosed, I'm following them up every three months for at least the first six

months generally, especially if I'm putting them on systemic therapy and then backing off and you know, really adjusting as the disease as the disease behaves.

Matt 59:44
Okay, so Mary Beth, this while Miss Otis is in the hospital, so we're admitting her, we're gonna step up her prednisone dose, any other things in the hospital that you need to do for her, whether it's in cardiac investigations or just keeping her on telemetry. Getting a baseline EKG, any other things that we should think about?

Mary Beth 1:00:04
I mean, we should I think if she's presenting with increased shortness of breath, we should think about cardiac, in addition to pulmonary, as well, as you know, potentially hematologic. So you get a CBC make sure her bone marrow is fine. She's not anemic things of that nature. And then you would check a cardiac evaluation. At the very least I have run telemetry, like you mentioned, and if there's anything and get an EKG, and if there's changes in her rhythm patterns, I think that would be an important reason to trigger a cardiac evaluation, I'd also probably get an echocardiogram. One thing that we haven't spoken much about is the component of pulmonary hypertension that occurs in sarcoid. And this can be a secondary to the parenchymal lung disease. So if they have severe enough parenchymal lung diseases can be secondary, but also, there is really, pulmonary hypertension specific to sarcoidosis, as such, so called group five pulmonary hypertension. And there's some literature supporting treating the pulmonary hypertension we see in sarcoid. So for that reason, I would get an echocardiogram, I would assess her pulmonary pressures, I would assess her cardiac function. And if I am those are off, consider cardiac involvement of sarcoid.

Matt 1:01:19
So it's, this has been fantastic. Definitely, we're leaving some stuff on the table. But we'll I'll ask each of you for one favorite take home point. JOHN, we'll start with you. And then and then back to Mary Beth.

John 1:01:36
I think the take home point really is about the amount of involvement that sarcoid you can have the variety of organ systems and just being thorough and looking for that sarcoid. That spurs the necessity of treatment. You don't want to miss neuro sarcoid. You don't want to miss cardiac-sarcoid. You don't want to miss pulmonary-sarcoid that's causing significant lung injury to a patient. So making sure that you're assessing your patient thoroughly. That's my number one thing, because it's so challenging to make sure that you're that you've covered your bases.

Mary Beth 1:02:11
Yeah, I would absolutely agree with that. And I would add to that just because of exactly what we said that that constant surveillance , that concern that it can involve any organ that. you have to remember that the patient burden is very high in this disease. It's high because there's, we as physicians are uncertain, we can't give them excellent prognostic information. It's high because they can have multiple organs involved and be running around doing a lot of tests. And its high because they suffer from impairment from the disease. So just being aware that our patients are suffering from this being alerted, you know, and being there for them I think is a very valuable take home point.

Paul 1:02:51
This has been another episode of the Curbsiders bringing you a little knowledge food for your brain.

Stuart 1:02:55
Oh, yummy.

Transcribed by MJ Allen, DO