Transcript Details
This is a transcript of a continuing medical education (CME) activity. Additional media formats for the activity and full activity details (including sponsor and supporter, disclosures, and instructions for claiming credit) are available by visiting:
https://reachmd.com/programs/cme/how-do-you-diagnose-and-assess-symptom-burden-when-non-advanced-systemic-mastocytosis-is-suspected/15628/

Released: 06/20/2023
Valid until: 06/20/2024
Time needed to complete: 1h 08m

ReachMD
www.reachmd.com
info@reachmd.com
(866) 423-7849

How Do You Diagnose and Assess Symptom Burden When Non-Advanced Systemic Mastocytosis Is Suspected?

Announcer:
Welcome to CME on ReachMD. This episode is part of our MinuteCE curriculum.

Prior to beginning the activity, please be sure to review the faculty and commercial support disclosure statements as well as the learning objectives.

Dr. Radia:
Hello, my name is Deepti Radia. I'm a Hematology Consultant at Guy's and St. Thomas' hospitals in London. Today I'm going to talk to you about How You Diagnose and Assess Symptom Burden When a Diagnosis of Non-Advanced or Indolent Systemic Mastocytosis is Suspected.

So the burden of mastocytosis is quite significant. Patients with indolent systemic mastocytosis, or SM, have a range of symptoms, as you can see reported on the right-hand side in 2016 from patients, which can be very variable, they can reflect the disease in their skin, leading to lots of urticarial pruritus, disease in their gut leading to lots of GI symptoms, cognitive impairment, abdominal pain, and bone pain. And those are just a few to mention. So the patients have to live with those mast cell-associated symptoms, the psychological burden of a chronic illness. And for those patients who have indolent disease, organ damage, in terms of osteoporosis, is quite a significant issue in their life leading to bone pain.

So symptoms and how have we measured them? In the past, it's essentially been listening to what the patient says. We have now move forward to developing symptom assessment tools or patient-reported outcomes, PROs. And the development of these symptom assessment forms is quite a challenge. So if you look at how the SM-SAF, ISM-SAF was developed, and that for advanced, but we'll focus on the ISM, a targeted population of patients, and a targeted population of experts within the field, and reviewed literature pulled out all the symptoms that had been discussed, noted, or commented on by patients. And as you can see in the middle box, these were huge. They cover all systems within the body, circulatory, clinical, brain, skin, gut, respiratory, anaphylactic-like, allergic-like, immune, systemic. So there are a significant number. And a symptom assessment form with all of these would be challenging. So the symptom assessment tools were based on harmonizing the literature, the patient and the expert concepts into developing symptom assessment forms that had certain items. And the ISM-SAF that's used within clinical trials has 11 items that, from the inventory, were most reported and most significant to most patients. The MC-QoL has more items, and the PGIS, the Patient Global Impression Symptom assessment form is similar. So all have variable numbers of items that patients need to comment on. And they're an objective measure of how that patient - how symptomatic that patient is, and how their disease impacts on their quality of life at that point in time when they fill out the form.

And you've got to remember from clinical practice, as well, that every single patient is unique. So this is just a picture to show you that if I see 3 patients who have an average tryptase level of between 20 and 40 micrograms per liter, every single patient will be completely different. You may have a patient with lots of gut symptoms, you may have a patient with lots of allergic types to multiple triggers, or you may have a patient who's completely asymptomatic and just has the diagnosis. But a significant proportion of patients can have a really high symptom burden, which will impact on their quality of life. Therefore, impact on their work performance, their productivity, their

mental, as well as their physical health.

So to highlight a patient case and put this into context, I was referred a 71-year-old Caucasian gentleman who worked as an industrial engineer when he was working, and he was sent for a specialist's opinion regarding management of his symptoms. And he was given - he had a diagnosis of indolent SM, and whether he was eligible for trial or not. His past medical history, he had a long history of chronic obstructive airways disease, yet interstitial lung disease mostly in his left lower lung, and he'd had a basal cell carcinoma removed earlier that year. In terms of his SM journey, 20 years previously to this, he was noted to have a widespread itchy rash, he noted it, he didn't really take much attention to it. But in 2016, he had back pain and it was found that he'd had a fracture of one of his lumbar vertebrae. It wasn't related to trauma. He had a DEXA scan carried out which confirmed he had significant osteopenia and he had degenerative disc disease, and it was severe in his lower lumbar spine and upper sacral spine. He was sent off for an endocrinology opinion in order to start him with bisphosphonates to treat his osteopenia and the fact that he'd had severe fractures. And in 2016, also because of the severe skin rash, and the fact that he was symptomatic, skin biopsy was carried out when he was referred to dermatologist, and a diagnosis of urticaria pigmentosa was made. He then was treated with narrow band UV light treatment, had 24 fractions which made a little bit of a difference and was given a combination of antihistamines and anti-mediator therapies, which gave him some discomfort. And then in 2019, from the dermatologist, he was referred to a hematologist, and a diagnosis of indolent SM was confirmed on a bone marrow biopsy that was carried out. And because he had persistent symptoms, and he had such intractable pruritis or itching, he was referred to us for our expert opinion.

Just bearing in mind when we saw him, his skin was really, really widespread rash, very irritable, he could not bear to wear much clothing that was close to him, he could only tolerate cool showers. He had acid reflux, he had weight loss and some loose motions. We know about the osteoporosis, and he had mild memory impairment and recall, but didn't never had any anaphylaxis. Clinically, he had congenital clubbing, but he had, more importantly for the diagnosis of indolent disease, he did not have any enlarged liver or spleen, and his rash was obvious. He was on the medications that are highlighted here, a combination of anti-HI and anti-H2 inhibitors and skin creams. And more importantly again, looking at the investigations, his full blood count parameters were within the normal range, he had a normal white cell differential, his blood film was normal, and his liver profile was normal. His tryptase was 71 micrograms per liter. Now we reviewed the bone marrow, which confirmed 4 out of 4 of the criteria to make the diagnosis of indolent SM. He had spindle-shaped mast cells seen in aggregates, he was positive for the C KIT D - sorry, the CD117 mast cell tryptase and CD25 C-KIT positive which is mutation that 95% of patients have the D816V, and his tryptase was greater than 20.

So we discussed the diagnosis, I changed his antihistamines. We up-titrated him, added more antihistamines that were long-acting, gave him instructions of how to increase those, we issued an EpiPen aspatients who have a 50% more chance of having an anaphylactic reaction despite not having had one just in case, and he was asked to keep a symptom diary. At that point, we were waiting to recruit into the PIONEER trial, and he was given a patient information sheet. Unfortunately, the pandemic arrived, and the trial was on hold till 2021 He had telephone call follow-ups.

So almost 18 months later, he came to our center again and was consented to take part in the trial. Moving at the symptom review at the baseline, he had increased fatigue and sleep disturbance, his itching was much worse, he had hot flushes. His feet were particularly bad, had burning sensation all the time, the top of his feet where the rash had got worse, the gut symptoms were stable, as were his cognitive impairment. And at this point he had up-titrated his antihistamines, and you can see how more added on. Again, the blood count and the liver function tests were normal, his tryptase was slightly higher at 102. And the screening bone marrow confirmed what we'd seen with his baseline previous bone marrow that he had a diagnosis of indolent systemic mastocytosis, the disease bulk of 15% on the trephine. And it's important at this point for me to note that when you measure a C-KIT, or you look for a C-KIT D816V mutation, you really must use a sensitive method like digital droplet PCR, as next generation sequencing is not sensitive enough, and it may miss a positive result.

So in terms of summary for this particular patient highlight, patients with indolent systemic mastocytosis can be extremely symptomatic, and their symptoms affect multiple body systems, affected by the mast cell-mediator release. This can be locally in the skin, locally in the gut or skeletal, or distally like the neuropsychiatric or cognitive symptoms, or can suffer from anaphylaxis, which our particular patient didn't. These can have a significant impact on quality of life, and significant numbers or multi-mediator therapy, anti-mediator therapy, and polypharmacy is often needed, but still doesn't manage the symptoms. The diagnostic investigations are really important to make the diagnosis of indolent SM, and we've talked about the relevance and the criteria needed for the bone marrow. And the C-KIT mutation which is a driver mutation, the D816V more than 90% of patients with systemic disease really needs a sensitive assay in order to be detected, as you can have low disease bulk.

Thank you.

Announcer:

You have been listening to CME on ReachMD. This activity is jointly provided by Global Learning Collaborative (GLC) and TotalCME, Inc. and is part of our MinuteCE curriculum.

To receive your free CME credit, or to download this activity, go to ReachMD.com/CME. Thank you for listening.